



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Timothy A. Coleman

Docket No.: PF112P6

Application No.: 09/921,143

Group Art Unit: 1653

Filed: August 3, 2001

Examiner: Not Yet Assigned

For: Vascular Endothelial Growth Factor 2

SUBMISSION OF REPLACEMENT/SUBSTITUTE DRAWINGS

Attn: Draftsperson
Commissioner for Patents
Washington, DC 20231

Sir:

Applicants submit herewith replacement/substitute Figures 1A-31U (68 sheets) to replace Figures 1A-31G (47 sheets) as originally filed. Additional pages are due to reorganization of the drawings in order to comply with the margin requirements under 37 C.F.R. § 1.84. No new matter is introduced.

No fee is believed due for this submission. In the event that a fee is required in connection with this submission, please charge the required fee to Deposit Account No. 08-3425.

Respectfully submitted,

Melissa J. Pytel

Registration No. 41,512

HUMAN GENOME SCIENCES, INC.
9410 Key West Avenue
Rockville, Maryland 20850
(301) 610-5764
Attorney for Applicants

Dated: April 17, 2003

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FIG. 1A MATCH WITH FIG. 1B



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MATCH WITH FIG. 1A

361	AGATCTTGAAAAGTATTGATAATGAGTGGAGAAAGACTCAATGCATGCCACGGGAGGTG -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ TCTAGAACTTTCATAACTATTACTCACCTCTTCTGAGTTACGTACGGTGCCTCCACA I L K S I D N E W R K T Q C M P R E V C	420
421	GTATAGATGGGGAAAGGGAGTTGGAGTCGGACAAACACCTCTTAAACCTCCATGTG -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ CATATCTACACCCCTTCCTCAAACCTCAGCGCTGTTGTGAAGAAATTGGAGGTACAC I D V G K E F G V A T N T F F K P P C V	480
481	TGTCGGTCTACAGATGTGGGGTTGCTGCAATAGTGAGGGCTGCAGTCATGAACACCA -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ ACAGGCAGATGTCTACACCCCCAACGACGTTATCACTCCCGACGTACGTACTTGTGGT S V Y R C G G C C N S E G L Q C M N T S	540
541	GCACGGAGCTACCTCAGCAAGACGTATTGAAATTACAGTGCCTCTCTCAAGGCCCCA -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ CGTGCCTCGATGGAGTCGTTCTGCAATAAAACTTTAATGTCACGGAGAGAGGTCCGGGGT T S Y L S K T L F E I T V P L S Q G P K	600
601	AACCAGTAACAATCAGTTTGCCTCAATCACACTCCTGCCGATGCATGTCTAAACTGGATG -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ TTGGTCATTGTTAGTCAAAACGGTTAGTGTGAAGGACGGCTACGTACAGATTGACCTAC P V T I S F A N H T S C R C M S K L D V	660

MATCH WITH FIG. 1C

FIG. 1B

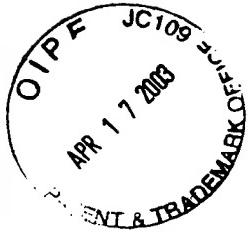


MATCH WITH FIG. 1B

661	TTTACAGACAAGTTCATTCCATTATTAGACGTTCCCTGCCAGCAAACACTACCACAGTGT -----+-----+-----+-----+-----+-----+-----+-----+-----+ AAATGTTCTGTTCAAGTAAGGTTAATAATCTGCAAGGGACGGTCTGTTGATGGTGTACAG Y R Q V H S I R R S L P A T L P Q C Q	720
721	AGGCAGCGAACAAAGACCTGCCAACCAATTACATGGAAATAATCACATCTGGCAGATGCC -----+-----+-----+-----+-----+-----+-----+-----+-----+ TCCGTCGCTTGTTCGGACGGGGTGGTTAATGTCACACCTTATTAGTGTAGACGGTCTACGG A A N K T C P T N Y M W N N H I C R C L	780
781	TGGCTCAGGAAGATTTATGTTTCCTCGGATGGCTGGAGATGACTAACAGATGGATTCC -----+-----+-----+-----+-----+-----+-----+-----+-----+ ACCGAGTCCTTCTAAATAACAAAGGACCCCTACGACCTCTACTGAGTTGTCTACCTAAAGG A Q E D F M F S S D A G D D S T D G F H	840
841	ATGACATCTGGGACCAAAAGGAGCTGGATGAAGAGACCTGTCAGTGTGTCAGAG -----+-----+-----+-----+-----+-----+-----+-----+ TACTGTAGACACCTGGTTGTTCTCGACCTACTTCTCTGGACAGTCACACAGACGTCTC D I C G P N K E L D E T C Q C V C R A	900
901	CGGGGCTTCGGCCTGGCCAGCTGGACCCCCAACAAAGAAACTAGACAGAAACTCATGCCAGT -----+-----+-----+-----+-----+-----+-----+-----+ GCCCGAAGCCGGACGGTCGACACCTGGGTCTCTGATCTGTCTTGTAGTACGGTCA G L R P A S C G P H K E L D R N S C Q C	960

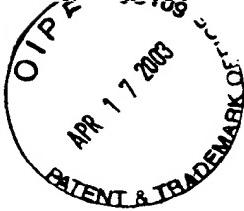
FIG. 1C

MATCH WITH FIG. 1D



MATCH WITH FIG. 1C

961	GTGCTGTAAAAACAAACTCTCCCCAGCCAATGGGGCAACCGAGAATTGATGAAA -----+-----+-----+-----+-----+-----+-----+-----+-----+ CACAGACATTGGTTGAGAAGGGTTCGGTTACACCCCGGTTGGCTCTAAACTACTTT V C K N L F P S Q C G A N R E F D E N	1020
1021	ACACATGCCAAGTGTATGTAAAAAGAACCTGCCAGAAATCAACCCCTAAATCCTGGAA -----+-----+-----+-----+-----+-----+-----+-----+-----+ TGTGTACGGTCACACATACTTACATTCTTGACGGGTCTTAGTTGGGATTAGGACCTT T C Q C V C K R T C P R N Q P L N P G K	1080
1081	AATGTGCCTGTGAATGTACAGAAAGTCCACAGAAATGCTTAAAGGAAAGGAAGTTC -----+-----+-----+-----+-----+-----+-----+-----+-----+ TTACACGGACACTTACATGTCTTCAGGTGTCTTACGAACAATTTCCTTCAAGG C A C E C T E S P Q K C L L K G K F H	1140
1141	ACCACCAAACATGCCAGCTGTTACAGACGCCATGTACGAACCGCCAGAAGGCTTGTGAGC -----+-----+-----+-----+-----+-----+-----+-----+-----+ TGGTGGTTGTACGGTGGACAATGTCTGCCGGTACATGCTTGGGGTCTTCCGAACACTCG H Q T C S C Y R R P C T N R Q K A C E P	1200
1201	CAGGATTTCATATAAGTGAAGAAGTGTGTCGGTTGTGTCCCTCATATTGGCAAAGACAC -----+-----+-----+-----+-----+-----+-----+-----+-----+ GTCTAAAGTATATCACTTCTTCACACAGCAACACAGGGAAAGTATAACCGTTCTGGTG G F S V S E E V C R C V P S Y W Q R P Q	1260



MATCH WITH FIG. 1D

AAATGAGCTAAGATGGTACTGTTTCCAGTTCATCGATTTCATCTATTATGGAAAACACTGTT TTTACTCGATTCTAACATGACAAAAGGTCAAGTAGCTAAAAGATAATACTTTTGACACA						
M S *						
TGCCACAGTAGAACACTGTCTGTAAACAGAGACCCTTGTGGGCCATGCTAACAAAGACA ACGGTGTCACTCTTGACAGACACTTGTCTCTCTGGGAACACCCCAGGTACGATTGTTCTGT	1321					
AAAGTCTGTCTTCCCTGAACCATGTGGATAACTTTACAGAAATGGACTGGAGCTCATCTG TTTCAGACAGAAAGGACTTGGTACACCTATTGAAATGTCTTACCTGACCTCGAGTAGAC	1381					
CAAAAGGCCTCTTGTAAAGACTGGTTCTGCCAATGACCAACAGCCAAGATTTCCTC GTTTCCGGAGAACATTCTGACCCAAAGACGGTTACTGGTTGTCGGTTCTAAAGGAG	1441					
TTGTGATTCTTAAAGAATGACTATAATTATTTCCACTAAAAATAATTGTTCTGC AACACTAAAGAAATTCTTACTGATATTAAATAAGGTGATTTTATAACAAAGAC	1501					
ATTCAATTATAGCAACAAATTGGTAAAACCTCACTGTGATCAATTATTTATATCAT TAAGTAAAATATCGTTGTTAACATTGAGTGACACTAGTTATAAAAATATAGTA	1561					
GCAAAATATGTTAAATAAAATGAAATTGTATTATAAAAAAAAAAAAAAA CGTTTTATACAAATTCTTATTCTTACTTTAACATAAATTTTTTTTTTTTTTTT	1621					

FIG 1E



FIG. 61 MATCH WITH FIG. 2B

**MATCH WITH FIG. 2A**

421 TGAATTACAGTGCCTCTCTCAAGGCCAAACCAGTAACAATCAGTTTGCCAATCA
- - +-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
E I T V P L S Q G P K P V T I S F A N H

481 CACTTCCTGCCGATGCCATGCTAAACTGGATGTTACAGACAAGTCATTCCATTATTAG
- - +-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
T S C R C M S K L D V Y R Q V H S I I R

541 ACGTTCCCTGCCAGCAAACACTAACAGTGTCAAGCAGCGAACAAAGACCTGCCACCAA
- - +-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
R S L P A T L P Q C Q A A N K T C P T N

601 TTACATGTGGAATAATCACATCTGCAGATGCCCTGGCTCAGGAAGATTATGTTTCCCTC
- - +-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
Y M W N N H I C R C L A Q E D F M F S S

661 GGATGCTGGAGATGACTCAACAGATGGATTCCATGACATCTGTGGACCAAAACAAGGAGCT
- - +-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
D A G D D S T D G F H D I C G P N K E L

721 GGATGAAGAGACCTGTCAGTGTCTGCCAGAGGGGGCTCGGCCCTGGCTGTGGACCC
- - +-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
D E E T C Q C V C R A G L R P A S C G P

MATCH WITH FIG. 2C**FIG. 2B**



MATCH WITH FIG-2B

EIG 2C

**MATCH WITH FIG. 2C**

1141	GTTCATCGATTTCATTATGGAAAACCTGTTGCCACAGTAGAACACTGTCTGTGAACAGA -----+-----+-----+-----+-----+-----+-----+-----+
1201	GAGACCCTGTGGGTCCATGCTAAACAAGACAAAAGTCTGCTTCTGAACCATGTGGA -----+-----+-----+-----+-----+-----+-----+-----+
1261	TAACTTACAGAAATGGACTGGAGCTCATCTGCAAAAGGCCCTCTTGTAAAGACTGGTTT -----+-----+-----+-----+-----+-----+-----+-----+
1321	CTGCCAATGACCCAAGATTTCCTCTGTGATTCTTTAAAGAATGACTATA -----+-----+-----+-----+-----+-----+-----+-----+
1381	TAATTATTCCACTAAAAATTGTGTTCTGCATTCAATTTATATGTTAAATAAACAAATTGGT -----+-----+-----+-----+-----+-----+-----+-----+
1441	AAAACCTCACTGTGATCAATATTCTTATATCATGCCAAATATGTTAAATAAACAAATTGAA -----+-----+-----+-----+-----+-----+-----+-----+
1501	TTGTATTATAAAAAAA -----+-----+-----+-----+-----+-----+-----+-----+



1 Pdgfa MRTLACLLL LGGCYLAHVL AEEAEIPREV IERLARSQIH SIRDLQRILLE
Pdgfb MNRCWA. LFL SLCCYLRVS AEGDPIEEL YEMLSDHSIR SFDDLQRLLH
Vegf MNFLL SWIVHWSALL LYLHHAKWSQA
Vegf2 MTV LYPEYWKKMYK CQLRKGCGWQHN

50

51 Pdgfa IDSVGSEDSL DTSLRAHCVH ATKHYPEKRP LPIRRKRSL EAVP
Pdgfb GDP.GEEDGA ELDLNMTRSH SGGELES. LARGRRSLG SLTIAEPAMI
Vegf APMAE GGCQ NHHEWVKFMD VYQR
Vegf2 REQANILNSRT ETIKFAAAH YNTIELKSID NEWRK.....

100

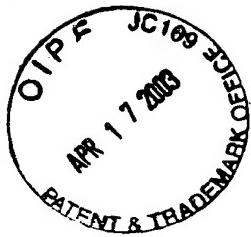
101 Pdgfa AVCKTRTVIY EIPRSQWDPT SANFLIWPPC VEVKRCTGCC NTSSVVKQOPS
Pdgfb AECKTRTEVF EISRRLIDRT NANFLVWPPC VEVQRCSGCC NNRNVQCRPT
Vegf SYCHPIETLV DIFQEYPDEI .. YIFKPSV VPLMRCGGCC NDECLEQVPT
Vegf2 TOQMPREVC1 DVGKEFGVAT .. NTFFKPPC VSVYRCCGC NSECLQMT

150

151 Pdgfa RVHHRSVKVA KVEYRKPK LKEVQVRLEE HLE6AC AT
Pdgfb QVQLRPVQVR KIEYRKPKI FKKATVTLED HLAC ETVAAPRVVT
Vegf EESNITMQIM RIK.PH. QC QHIGEMSFLQ HNKCECRPKK DRARQEKKSV
Vegf2 STSYLSKTLF EIT.VPLSOG PKPVTISAN HTSGCQMSKL DVYRQWHSII

200

FIG. 3A



201 Pdgfa TSLNPD YREEDT D VR.

Pdgfb RSPGGSQEQR AKTPQTRVTI RTVVRRRPK GKHRKFKHIT DKTALKETLG
Vegf RGK GKGQKRKRK K SRYKSWSY V GARCCLM PW SLPGPHP
Vegf2 RRSSUPATLPO CQAANKTCPT NYMMNNHICR CLAQEDFMFS SDAGDDSTDG250 Pdgfa
Pdgfb A
Vegf CGP
Vegf2 FHDICCPNKE LDEETCACVC RAGLRPASCC PHKEL...DR NSCCCVCKNK300 Pdgfa
Pdgfb A
Vegf CSE RRKHLFVQDP QTCKCSCKNT
Vegf2 FHDICCPNKE LDEETCACVC RAGLRPASCC PHKEL...DR NSCCCVCKNK350 Pdgfa
Pdgfb DSRCKARQ LELNERTCRC DKPRR
Vegf EFDENTCQC VCKRTCPRNQ PLNPCKCACE CTE SPQKCLL
Vegf2 LFPSQCCANR398 Pdgfa
Pdgfb
Vegf
Vegf2 KGKKFHHTC SCYRRPCTNR QKACEPGFSY SEEVCRCVPS YWQRQMS

FIG. 3B



**PERCENTAGE (%) OF AMINO ACID IDENTITIES BETWEEN
EACH PAIR OF GENES IS SHOWN IN THE
FOLLOWING TABLE**

	PDGF α	PDGF β	VEGF	VEGF-2
PDGF α				
PDGF β	48.0			
VEGF	20.7	22.7		
VEGF-2	23.5	22.4	30.0	

FIG. 4

Expression of VEGF2 mRNA in Human Breast Tumor Cells



- Lane 1. normal breast tissue
- Lane 2. breast tumor tissue
- Lane 3-9. breast tumor cell lines.

FIG. 5



Expression of VEGF-2 mRNA in Human Adult Tissues

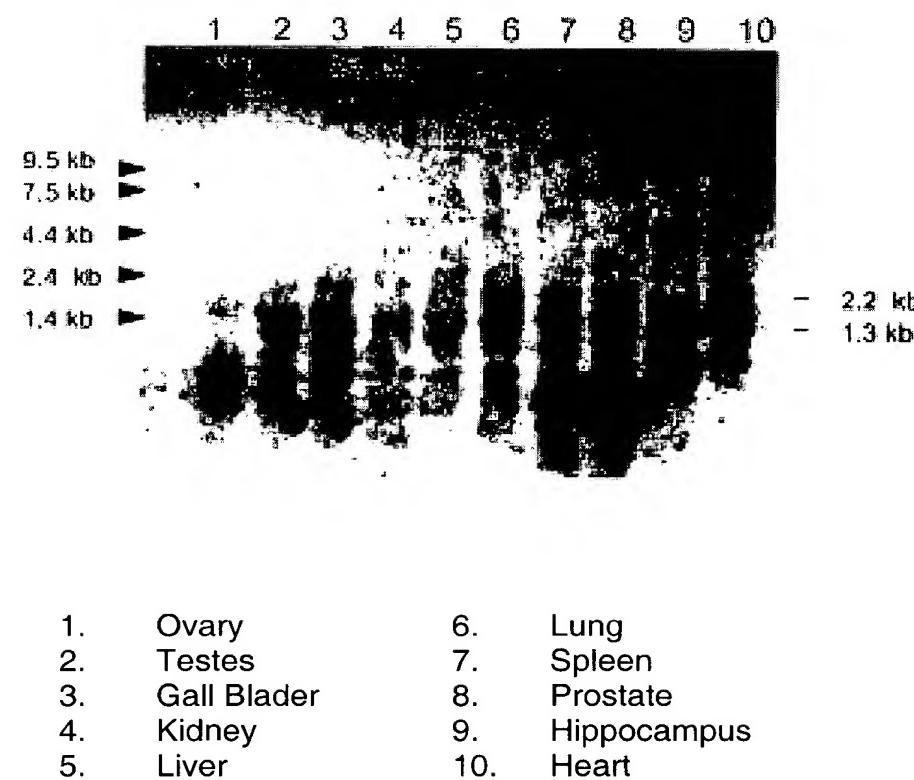
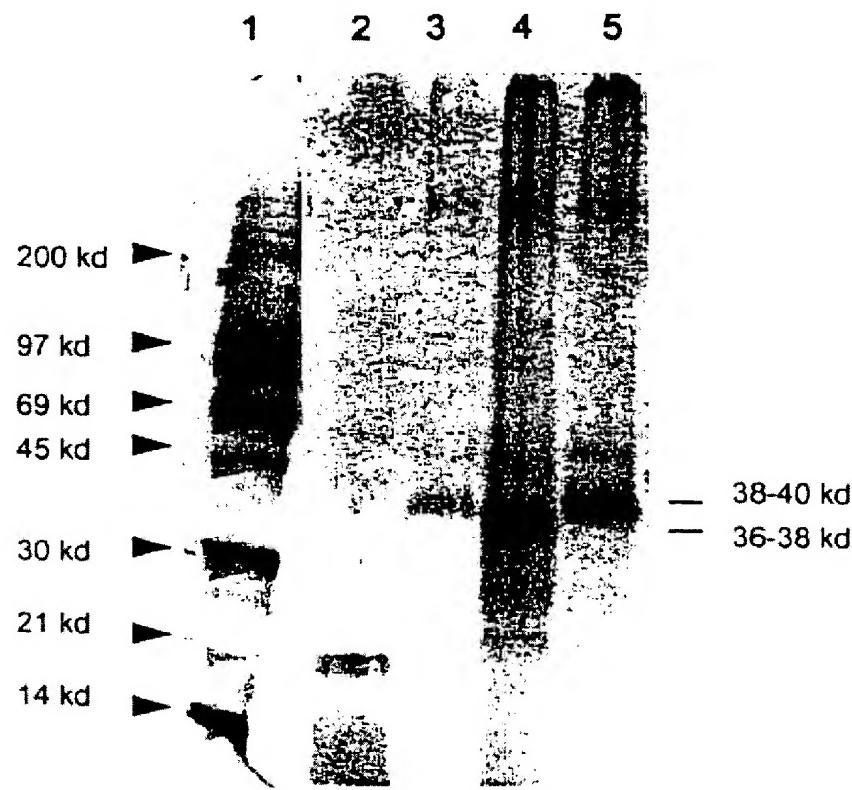


FIG. 6

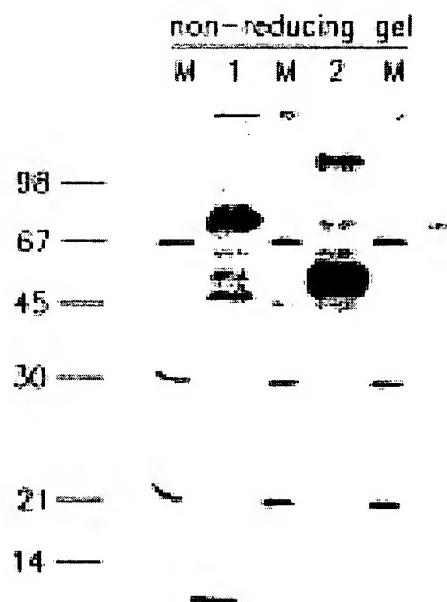


- Lane 1: 14-C and rainbow M.W. marker
Lane 2: FGF control
Lane 3: VEGF2 (M13-reverse & forward primer)
Lane 4: VEGF2 (M13-reverse & VEGF-F4 primer)
Lane 5: VEGF2 (M13-reverse & VEGF-F5 primer)

FIG. 7

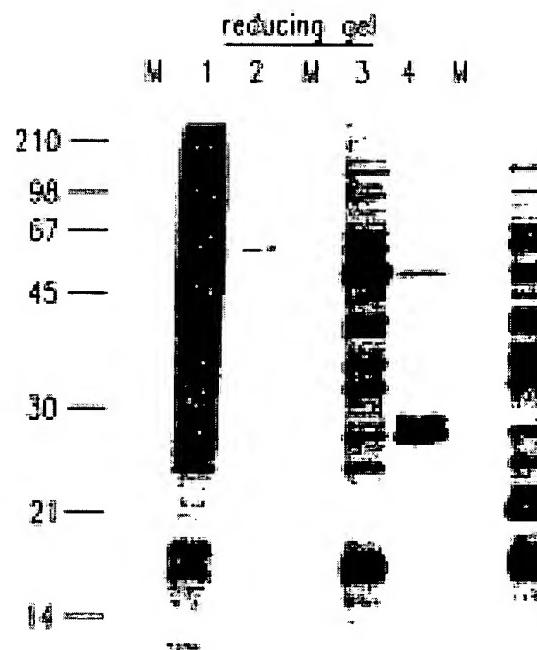
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Lane M: Marker
Lane 1: Vector medium
Lane 2: VEGF2 medium

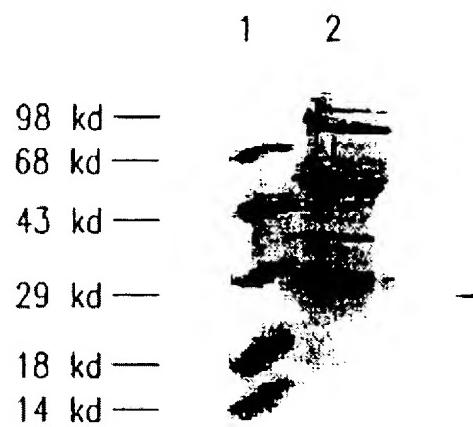
FIG. 8A



Lane M: Marker
Lane 1: vector cytoplasm
Lane 2: vector medium
Lane 3: VEGF2 cytoplasm
Lane 4: VEGF2 medium

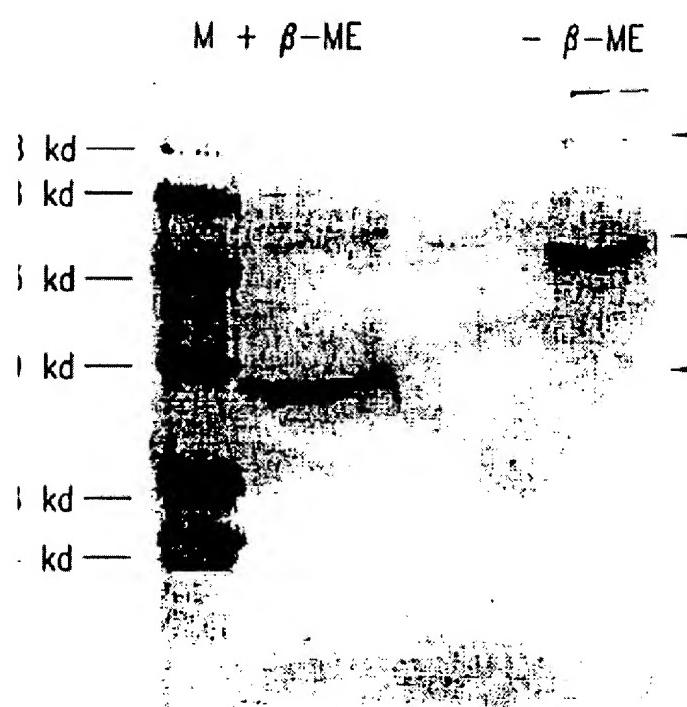
FIG. 8B

FIG. 9



Lane 1: Molecular weight marker
Lane 2: Precipitates containing VEGF2.

FIG. 10



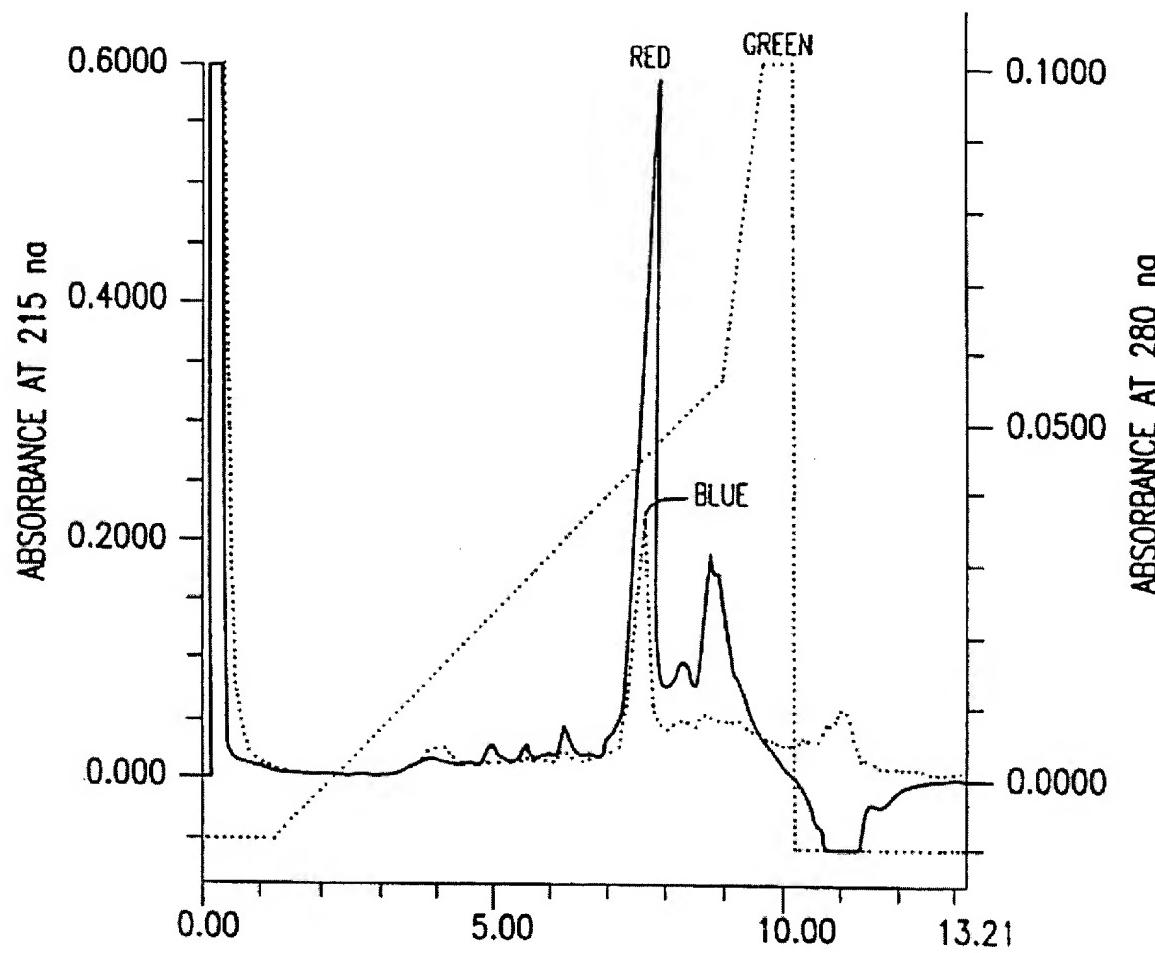


FIG. 11

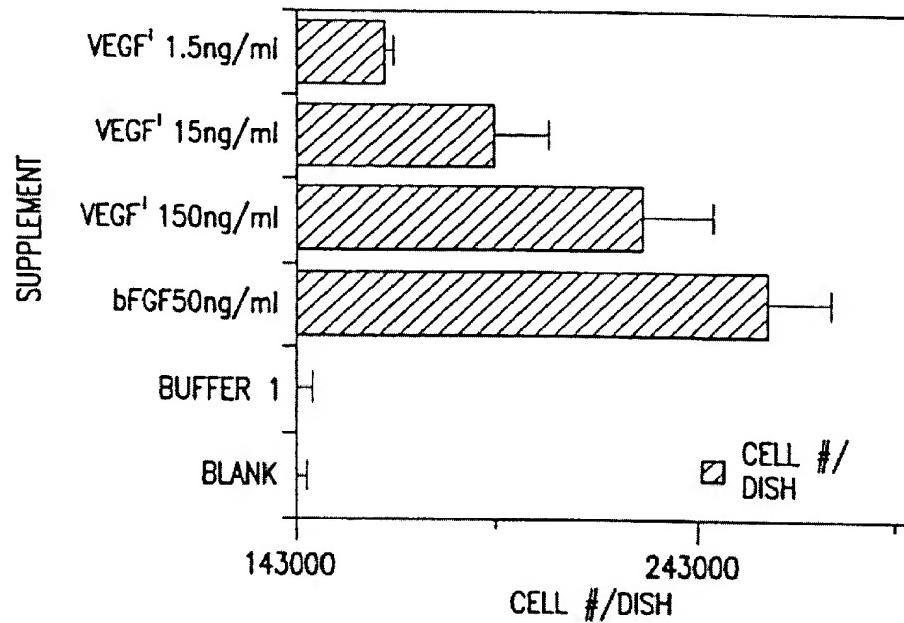


FIG. 12

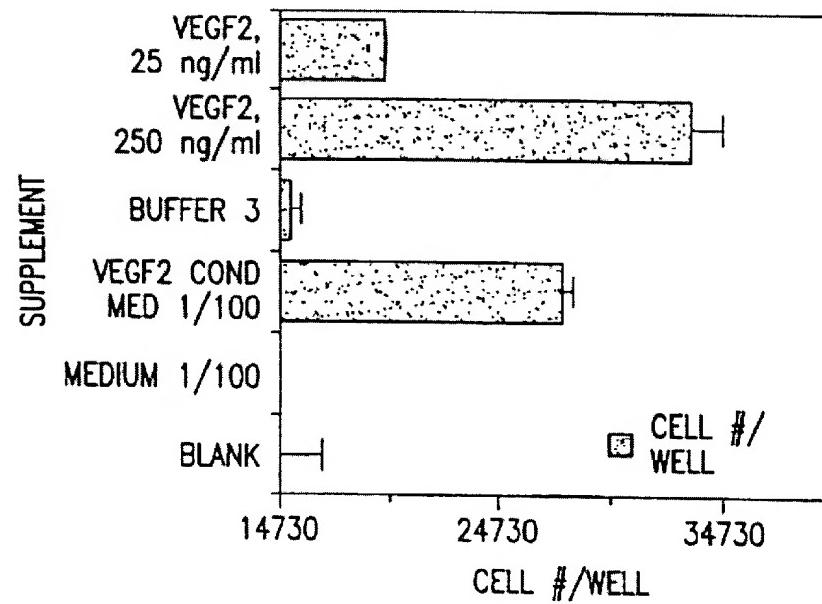


FIG. 13



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fetal kidney	fetal lung	fetal liver	brain	kidney	lung	liver	spleen	thymus	bone marrow	testes	placenta	skeletal muscle
1	2	3	4	5	6	7	8	9	10	11	12	13

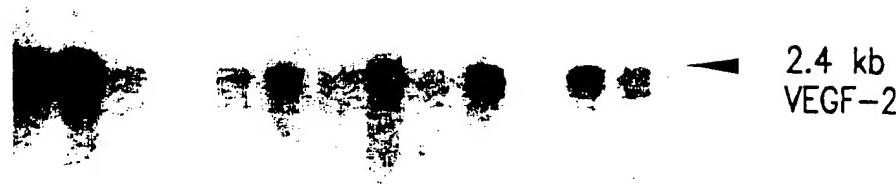


FIG. 14A

M B 1 2 3 4 5 6 7 8 9 10 11 12 13

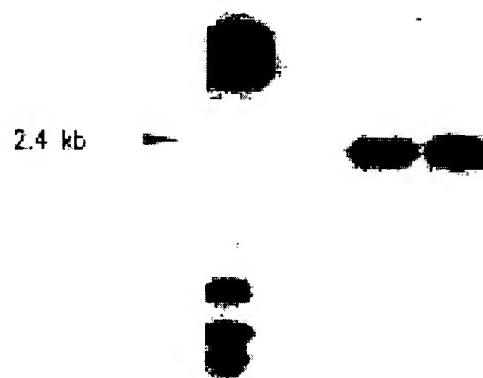


FIG. 14B

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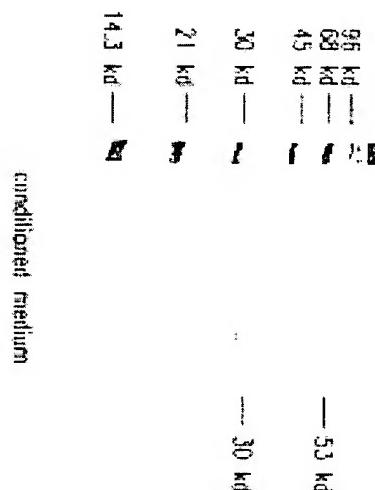
1 2 3 4 5 6



1. Molecular weight marker
2. Umbilical vein endothelial cells
3. Aortic smooth muscle cells
4. Dermal fibroblast

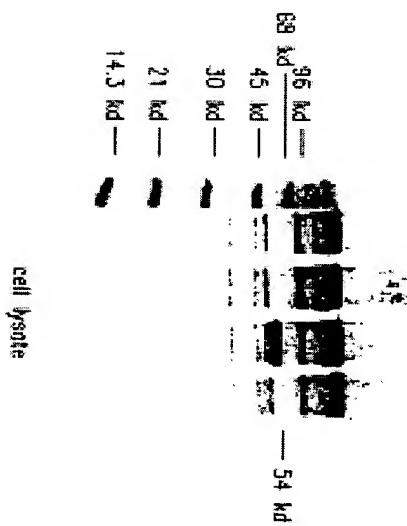
FIG. 15

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1. Molecular weight marker
2. Blank
3. Control protein-HA
4. Vector control
5. VEGF2-HA

FIG. 16A



1. Molecular weight marker
2. Blank
3. Control protein-HA
4. VEGF2-HA
5. Vector control

FIG. 16B

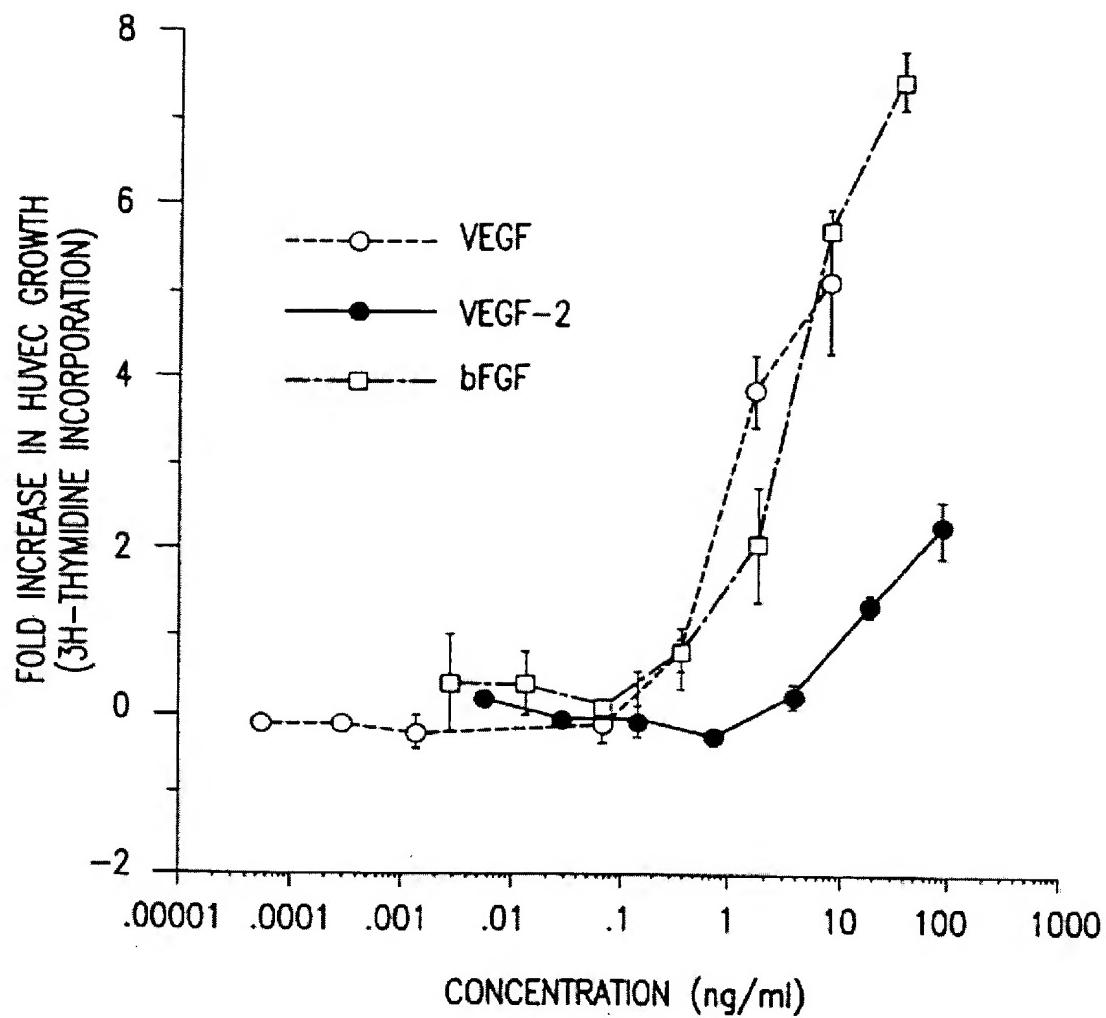


FIG. 17

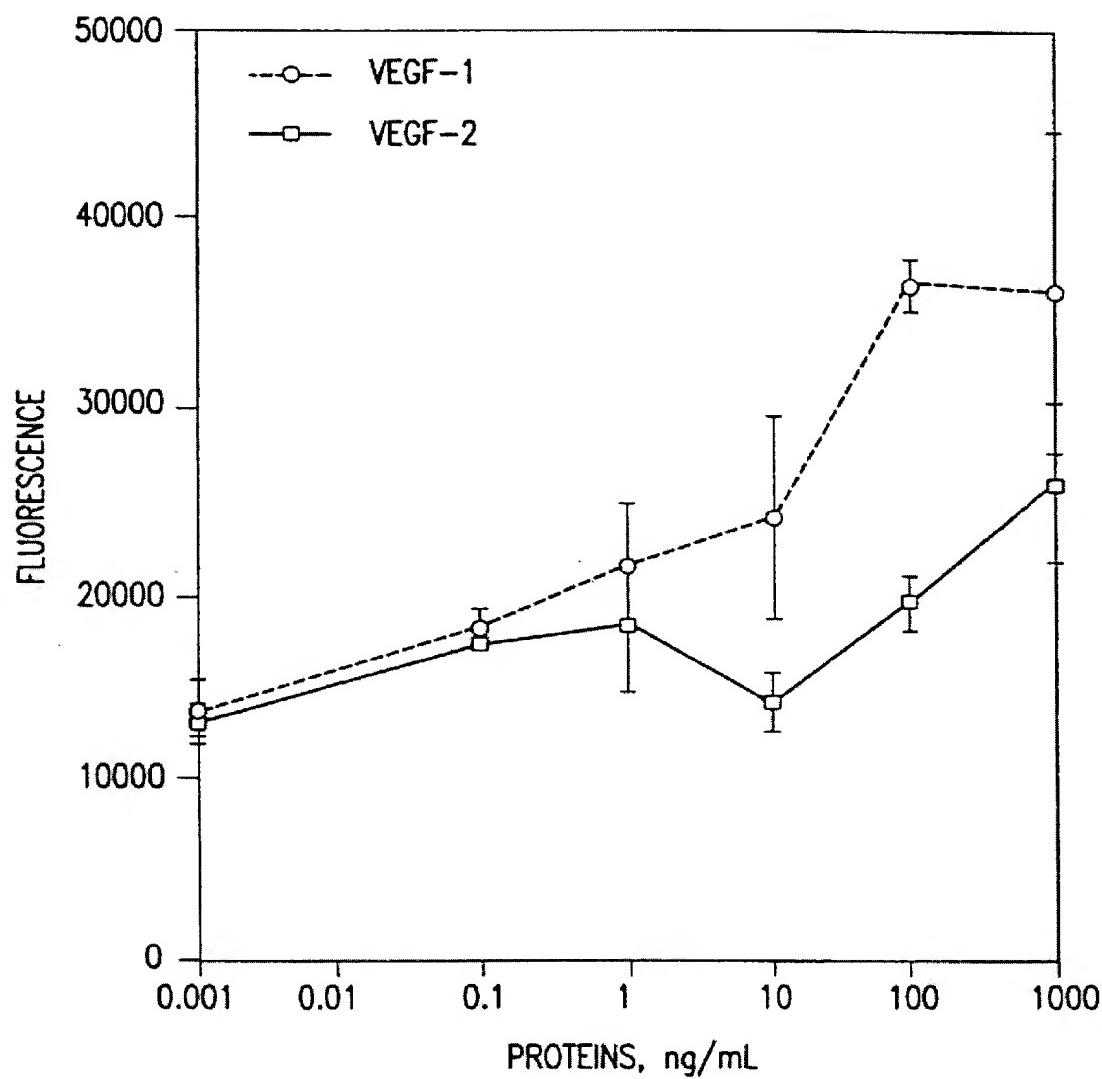


FIG. 18

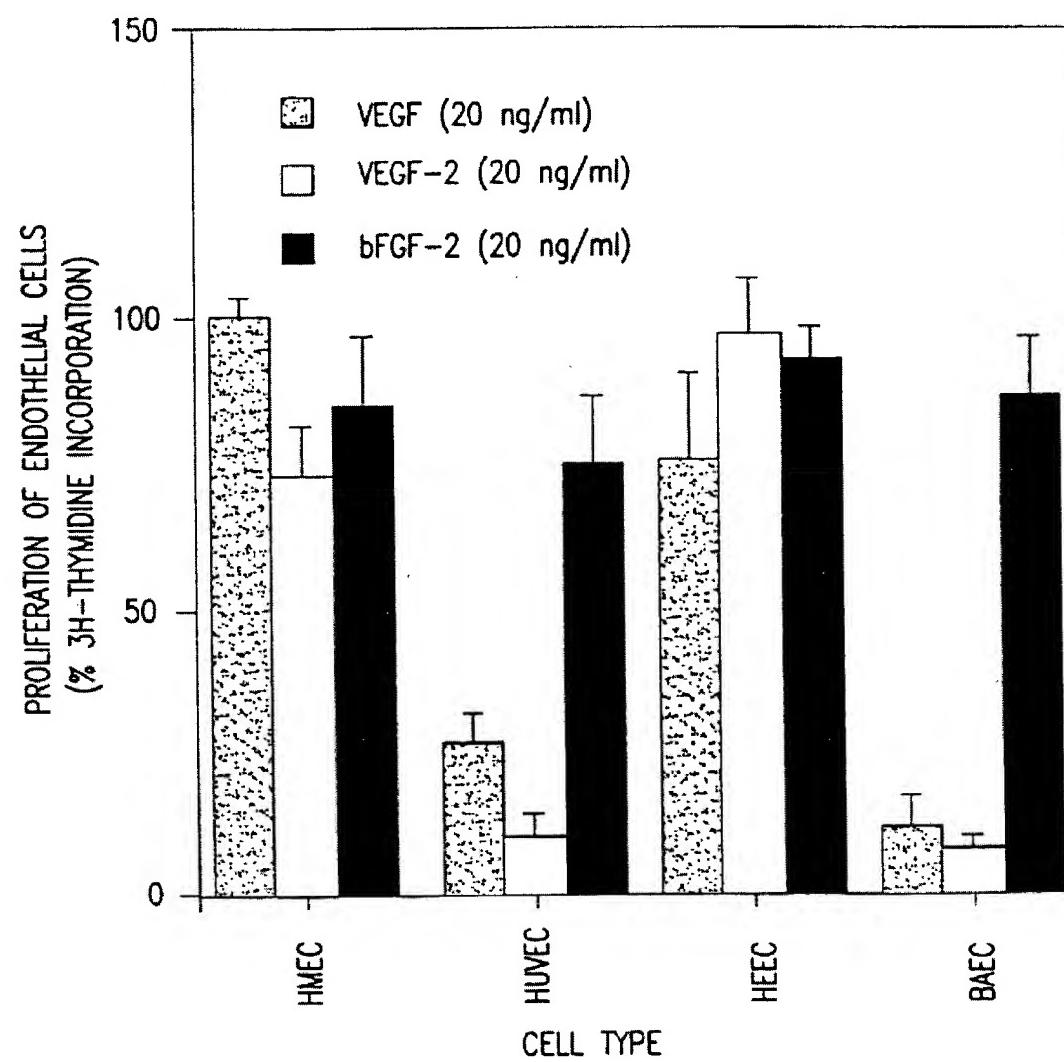


FIG. 19

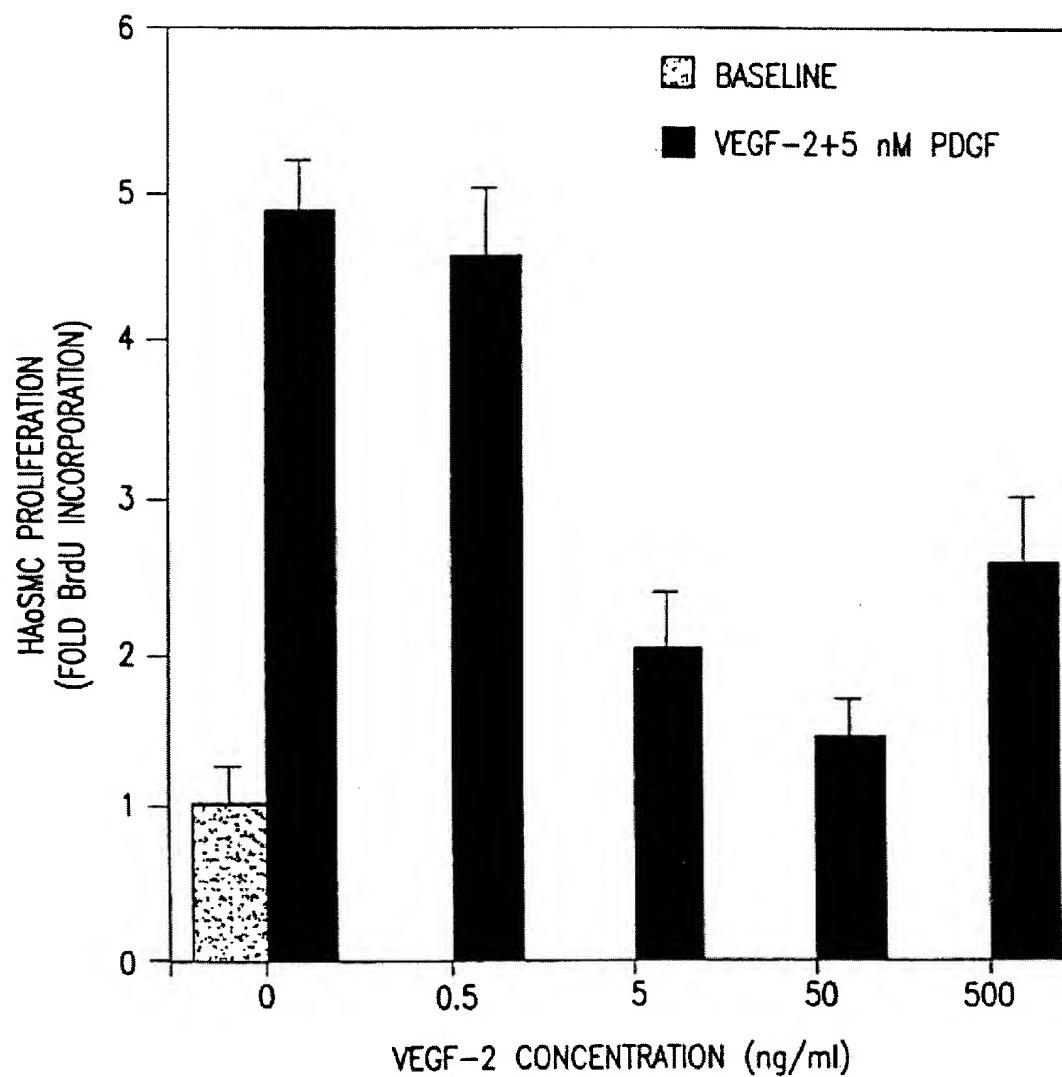


FIG. 20A

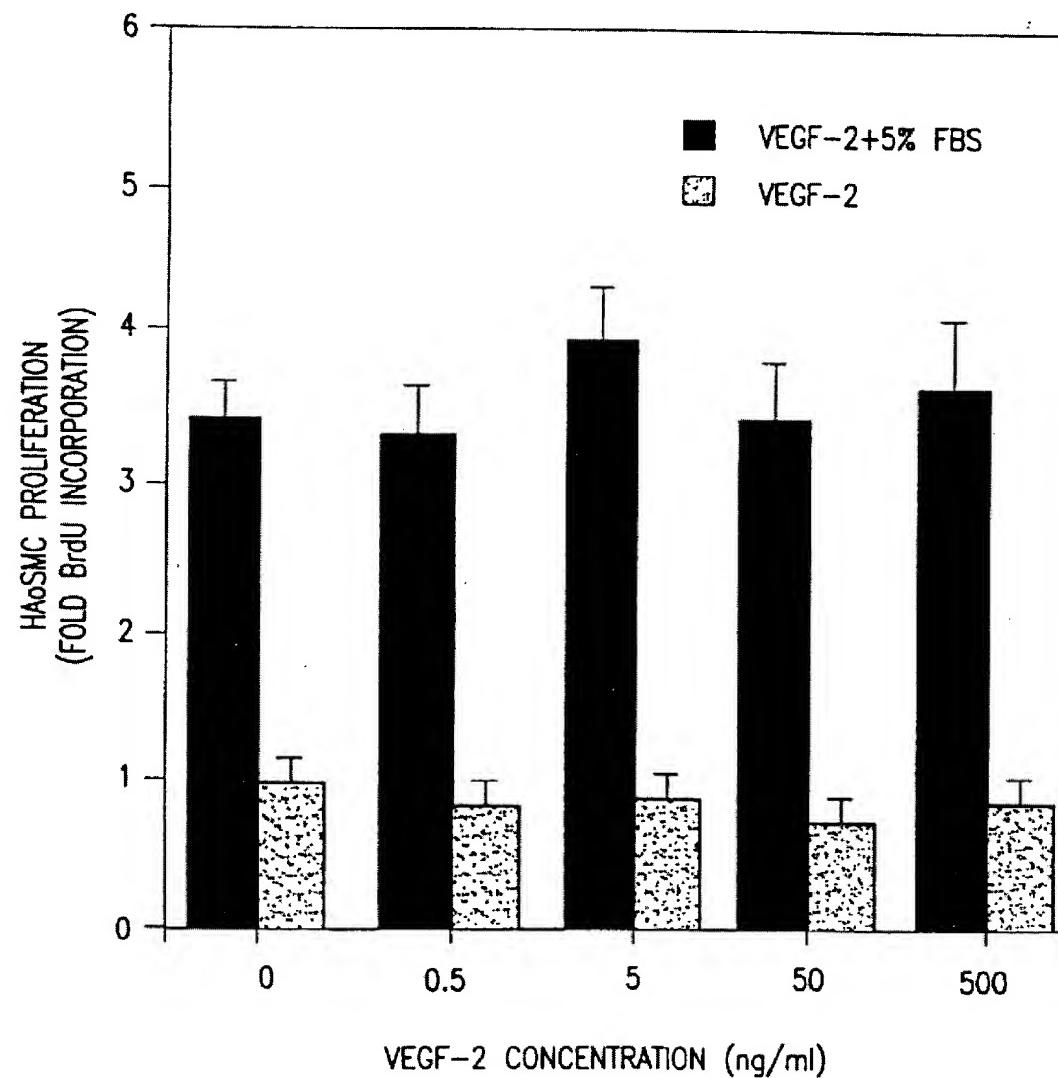


FIG. 20B

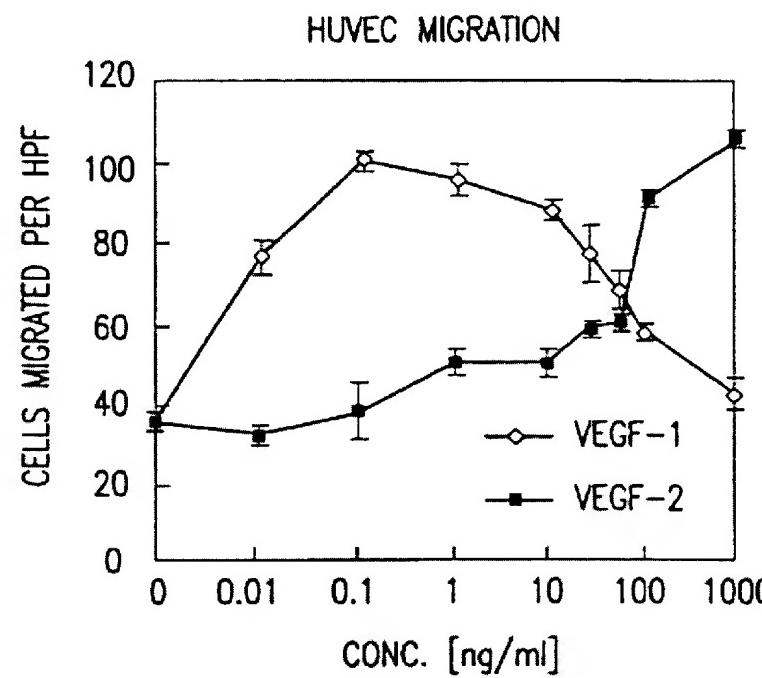


FIG. 21A

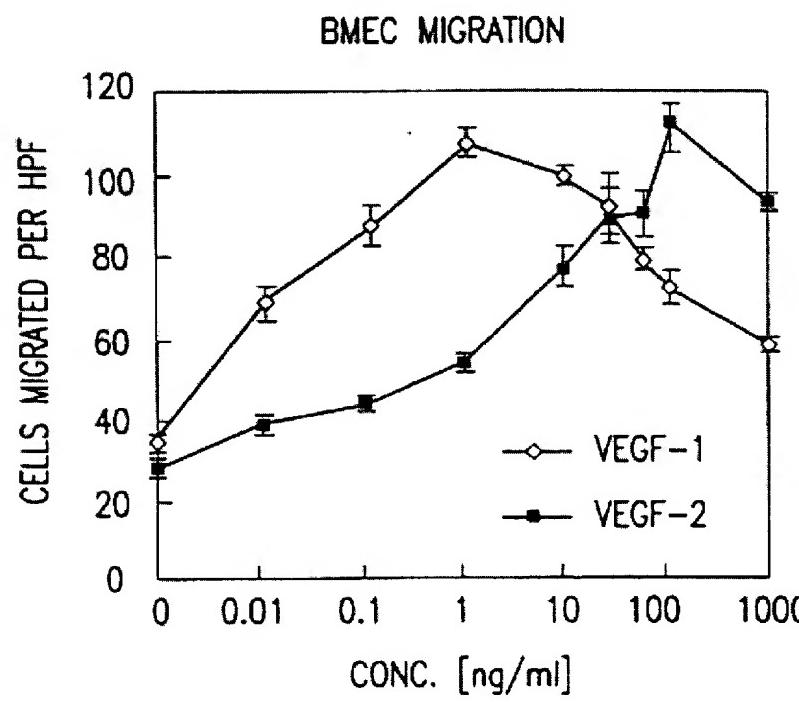


FIG. 21B

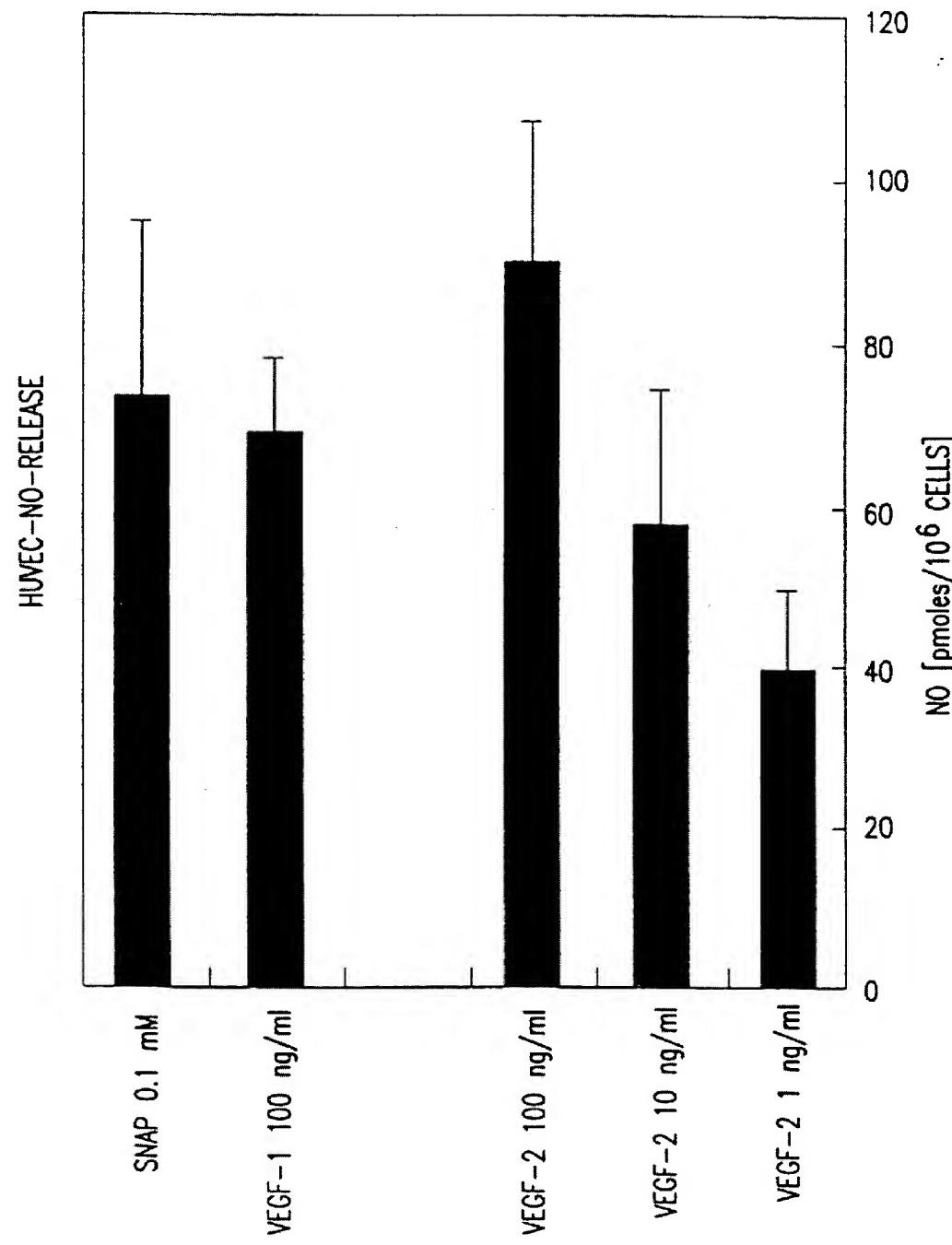


FIG. 22

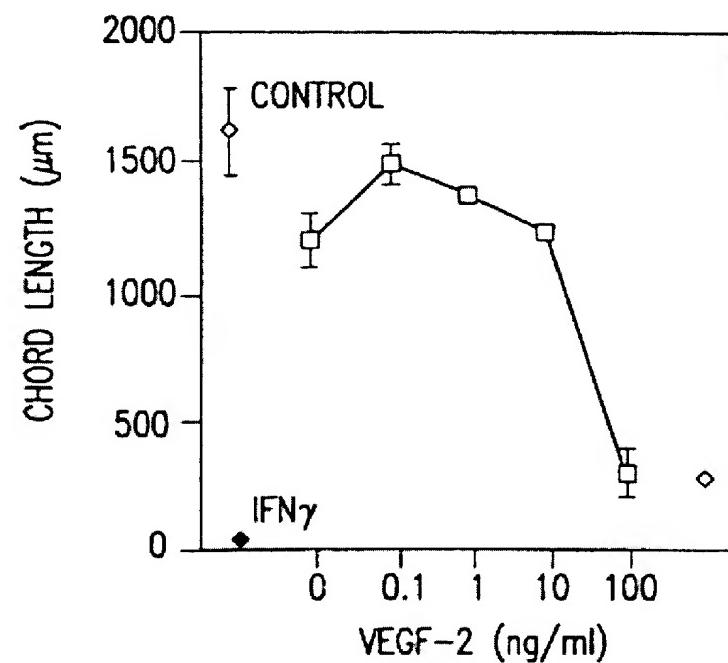


FIG. 23

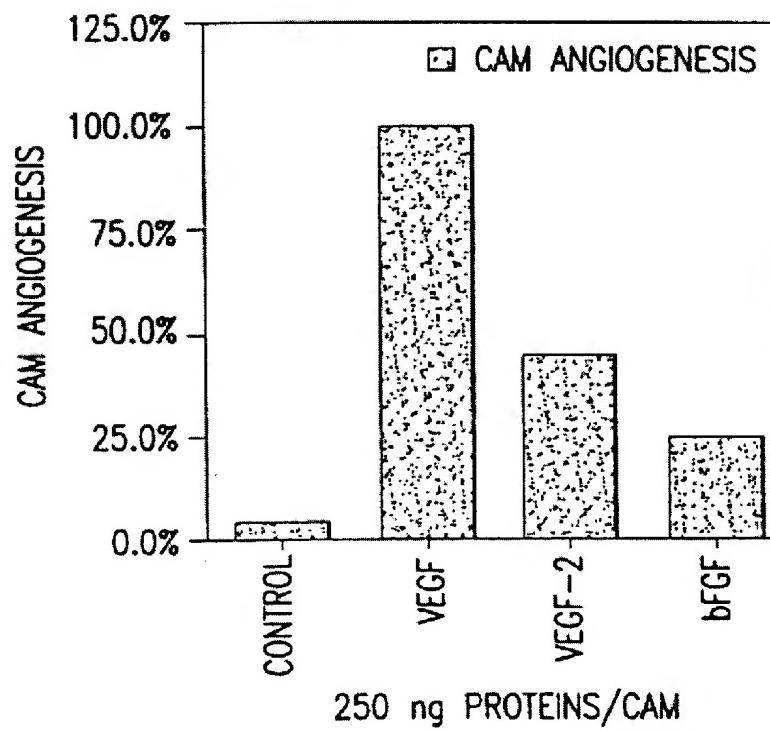


FIG. 24

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CALF BLOOD PRESSURE RATIO
-PROTEIN I.A.-

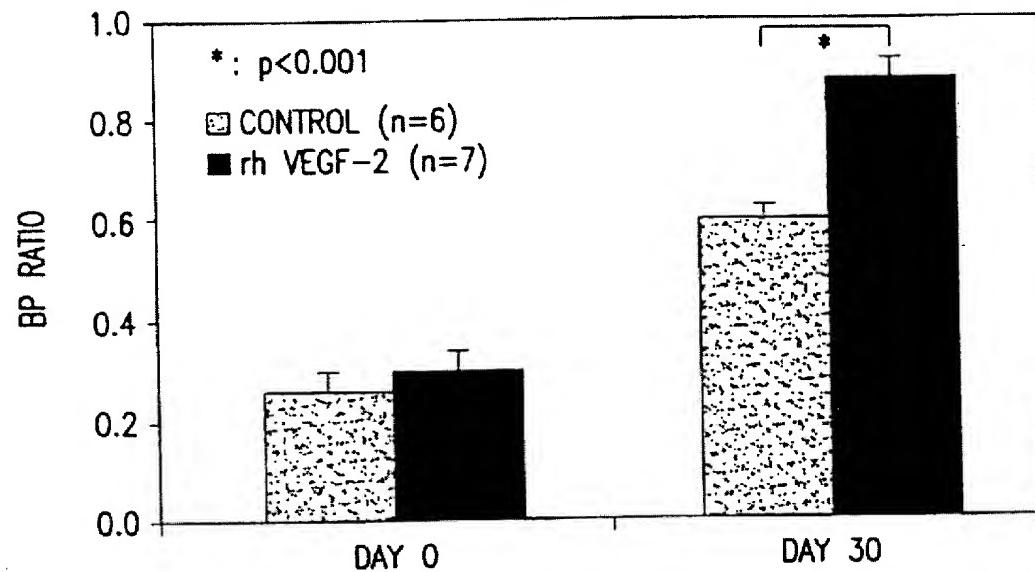


FIG. 25A

CALF BLOOD PRESSURE RATIO
-PLASMID-

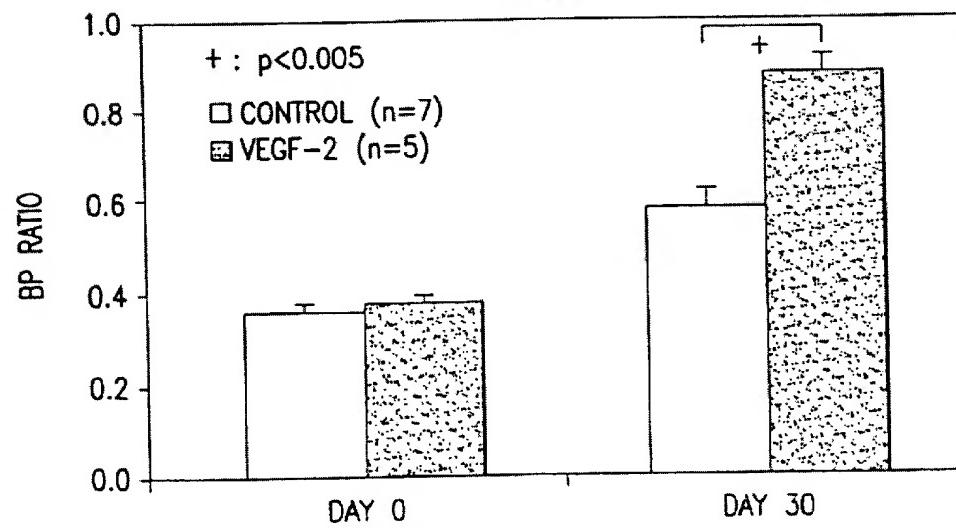


FIG. 25B

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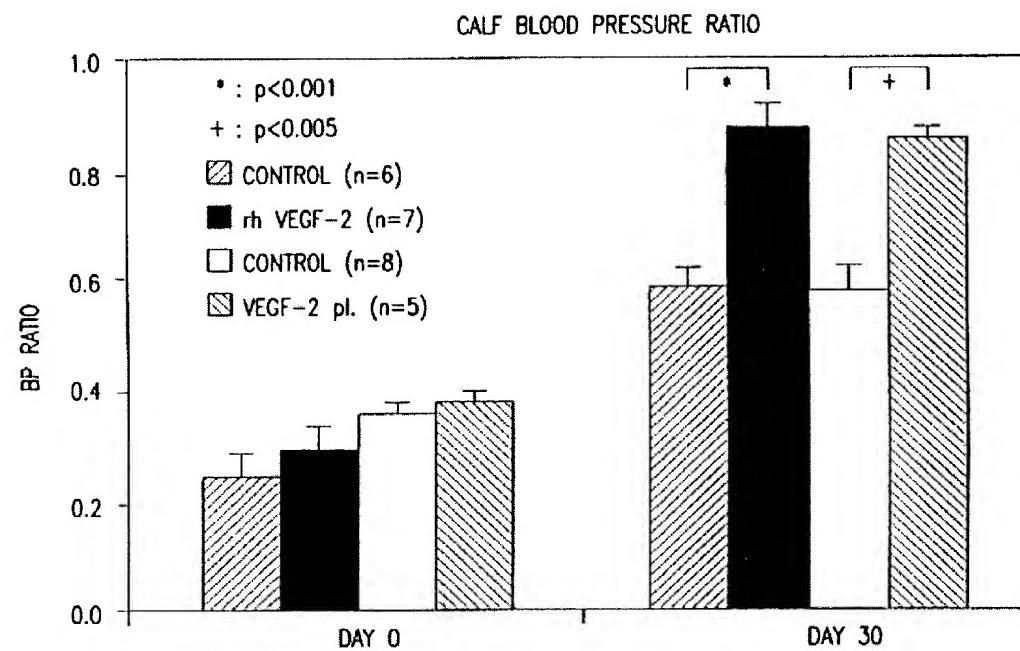


FIG. 25C

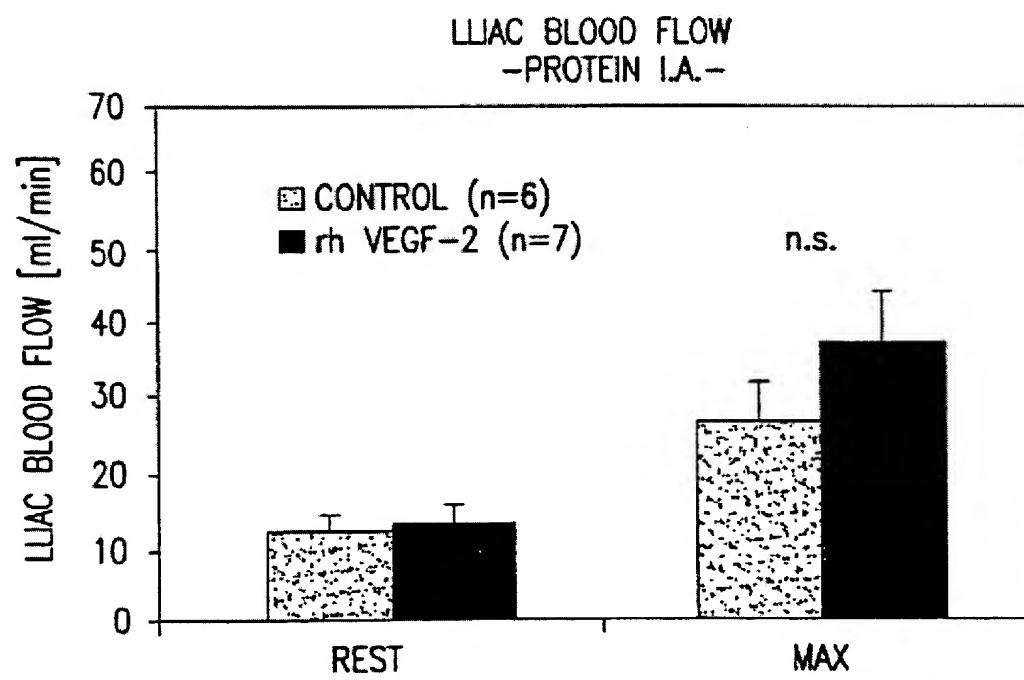


FIG. 25D

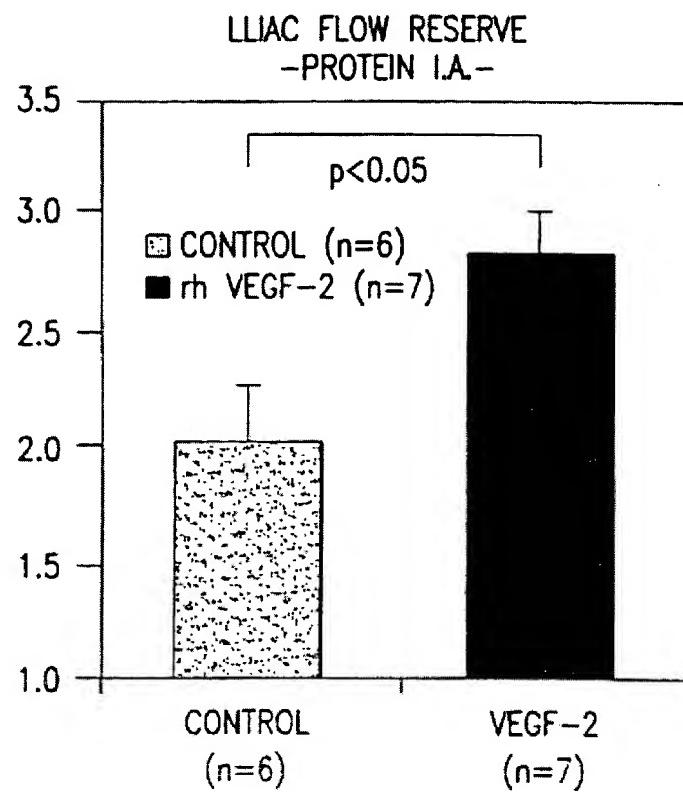


FIG. 25E

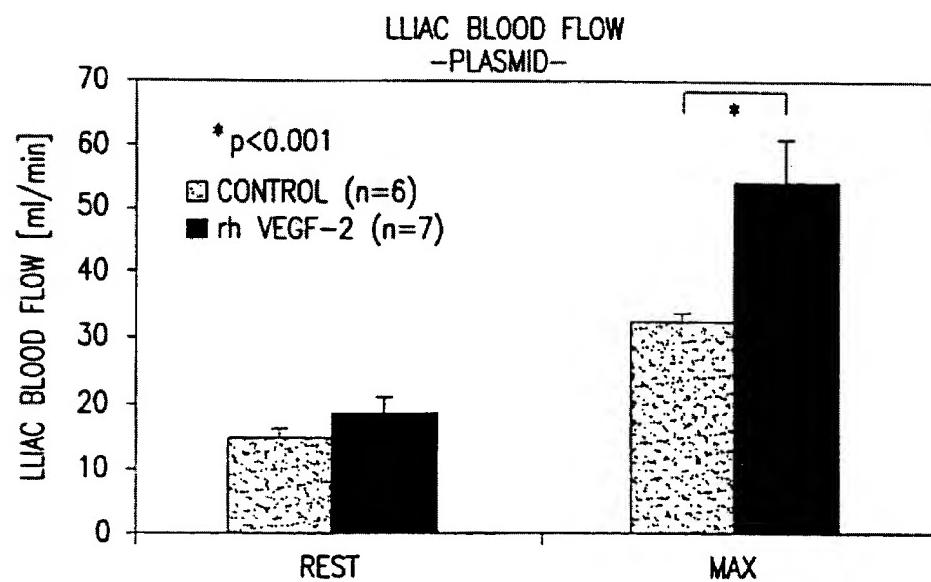


FIG. 25F

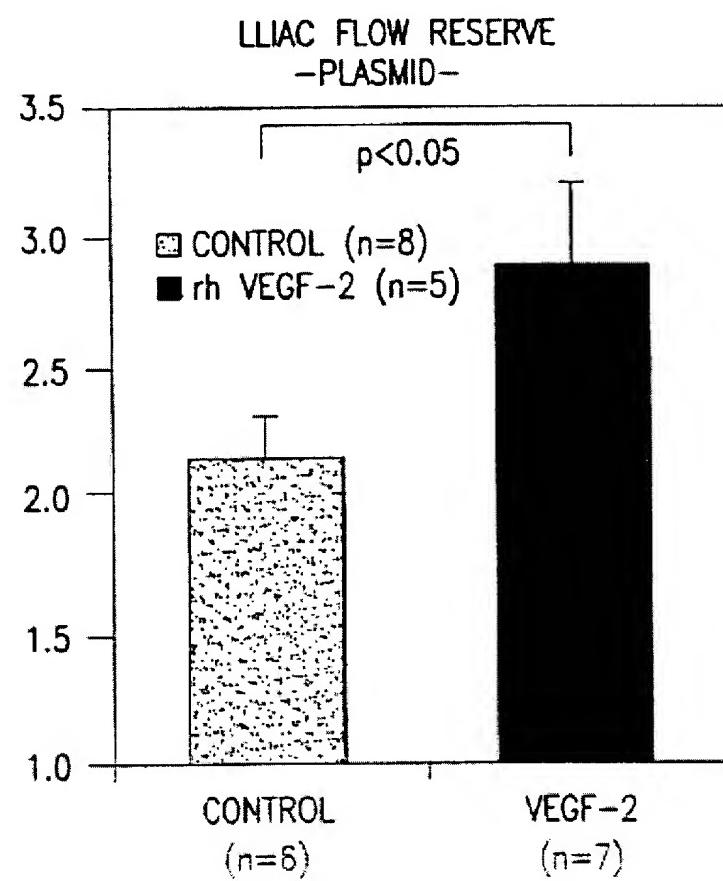


FIG. 25G

LLIAC BLOOD FLOW

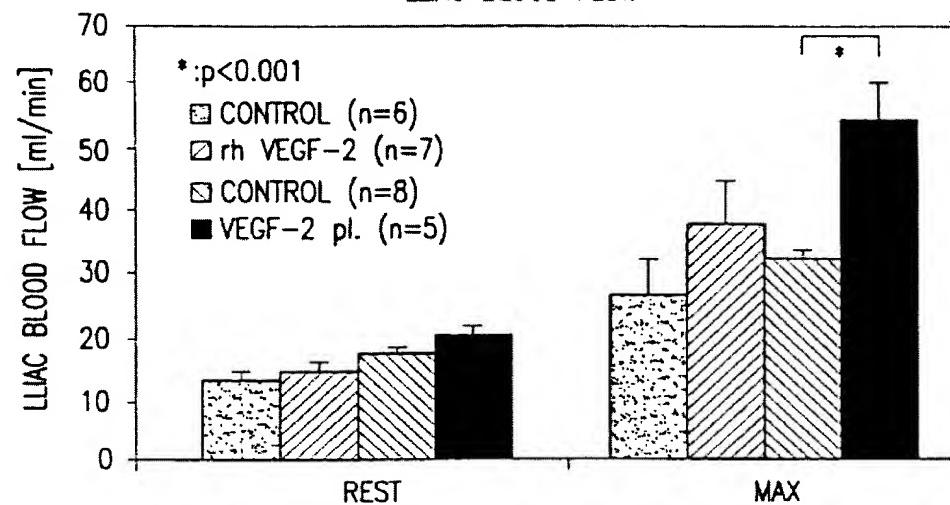


FIG. 25H

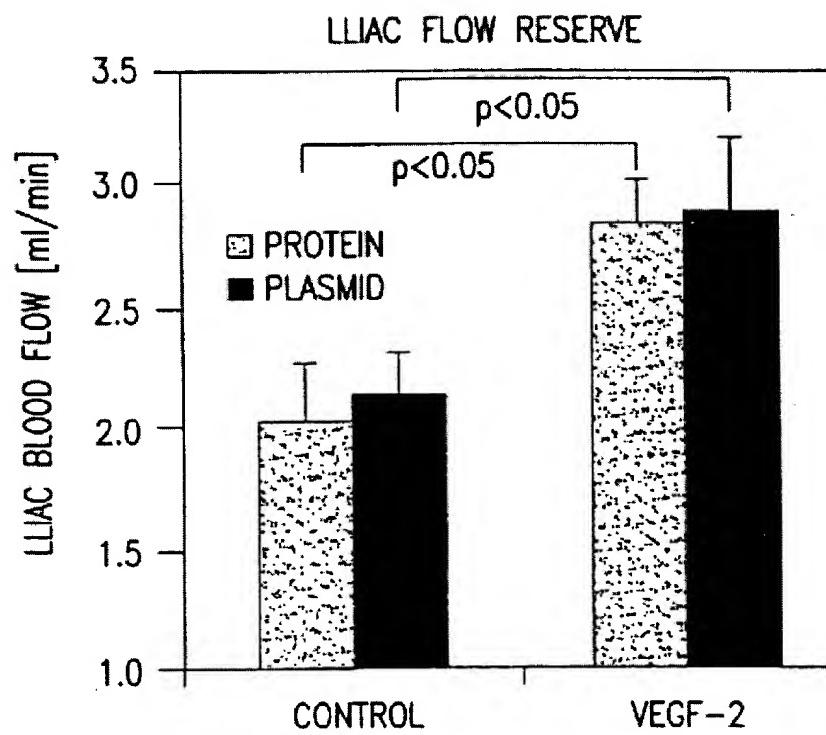


FIG. 25I

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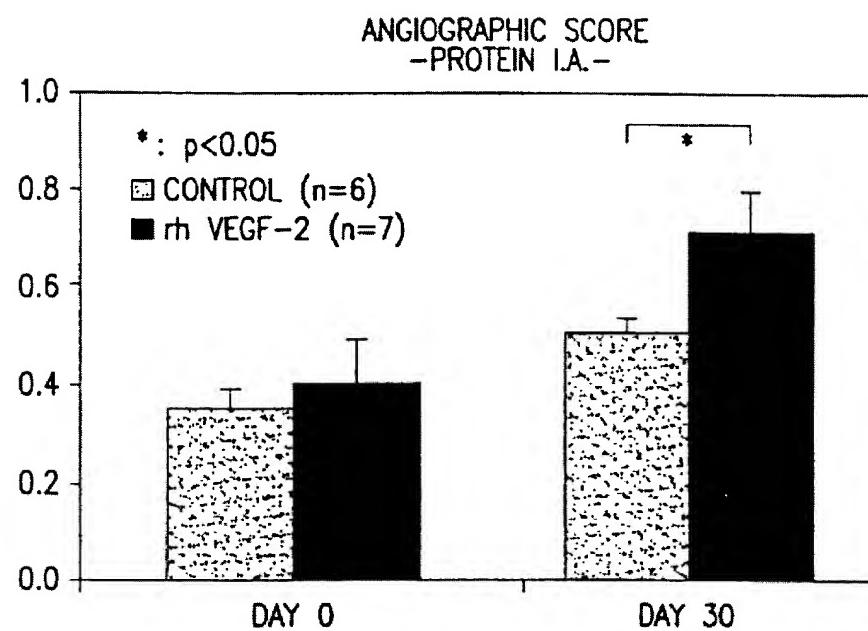


FIG. 25J

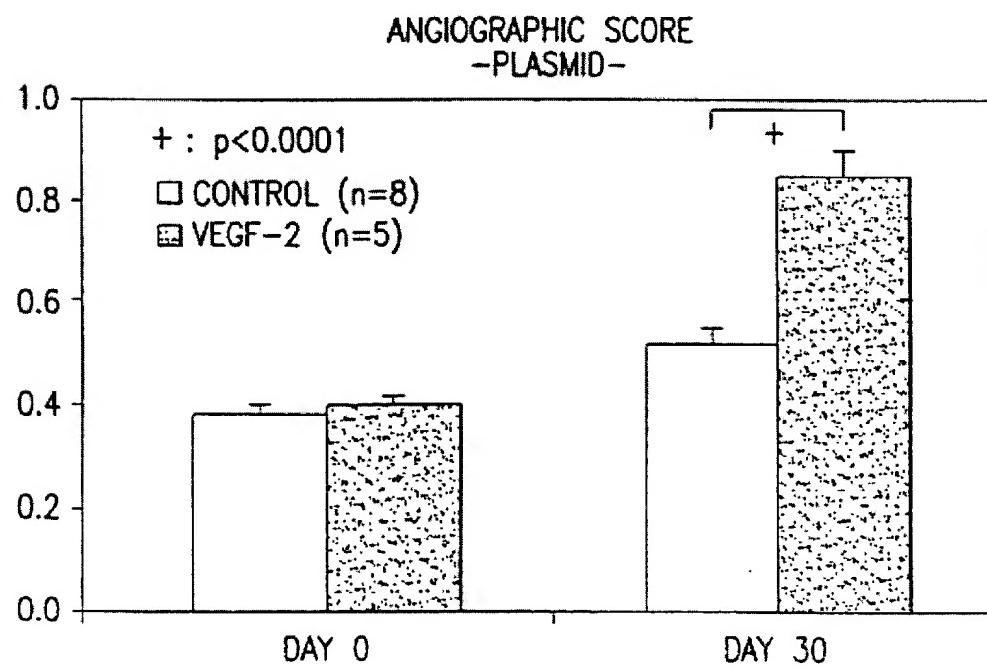


FIG. 25K

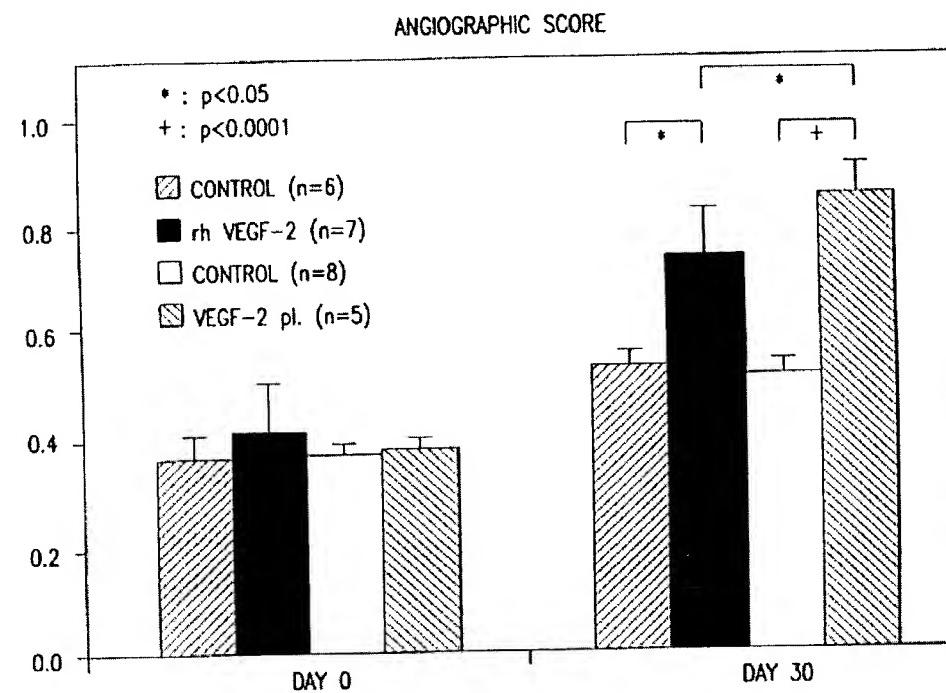


FIG. 25L

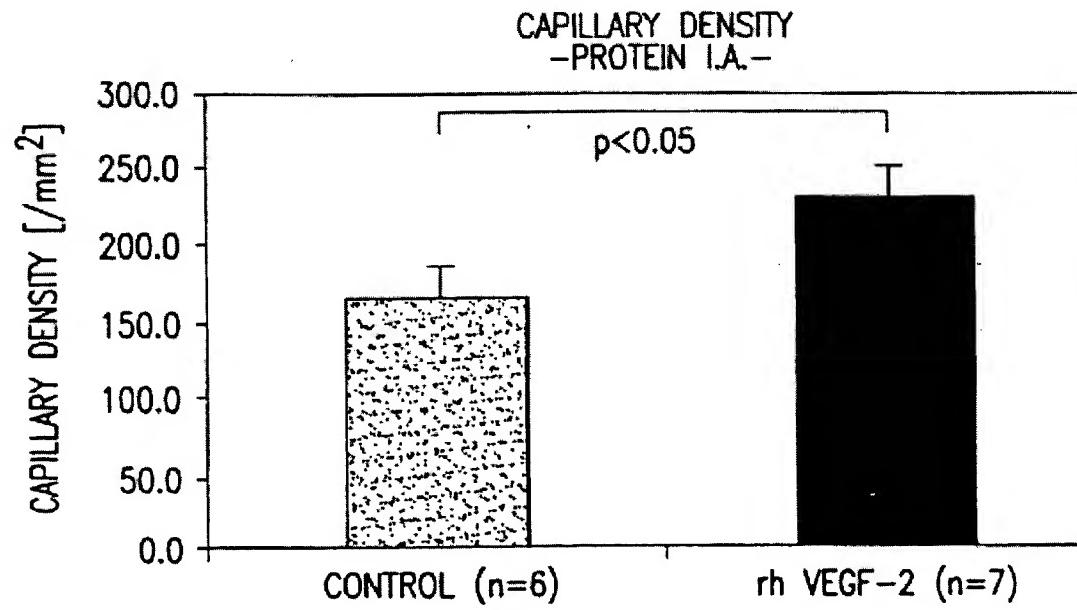


FIG. 25M

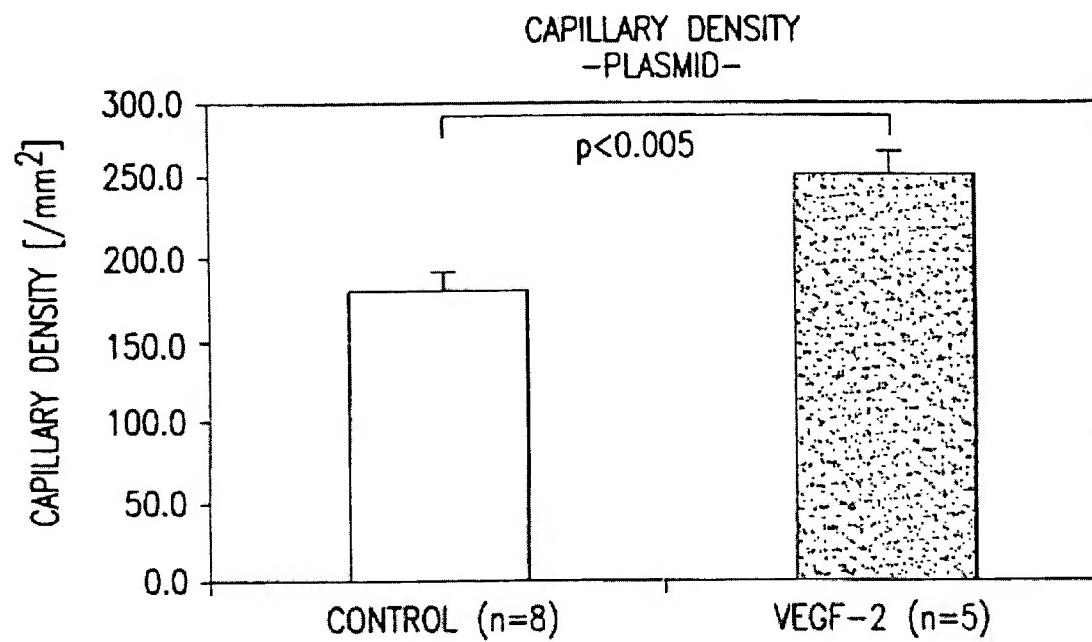


FIG. 25N

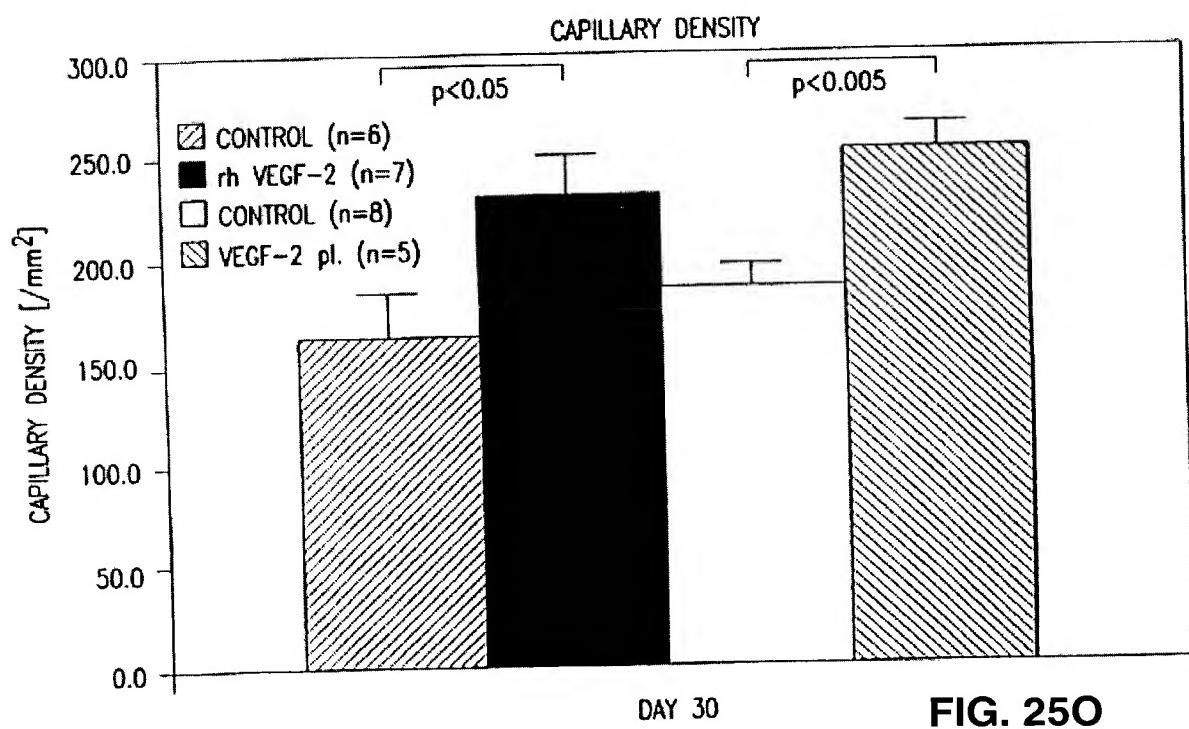


FIG. 25O

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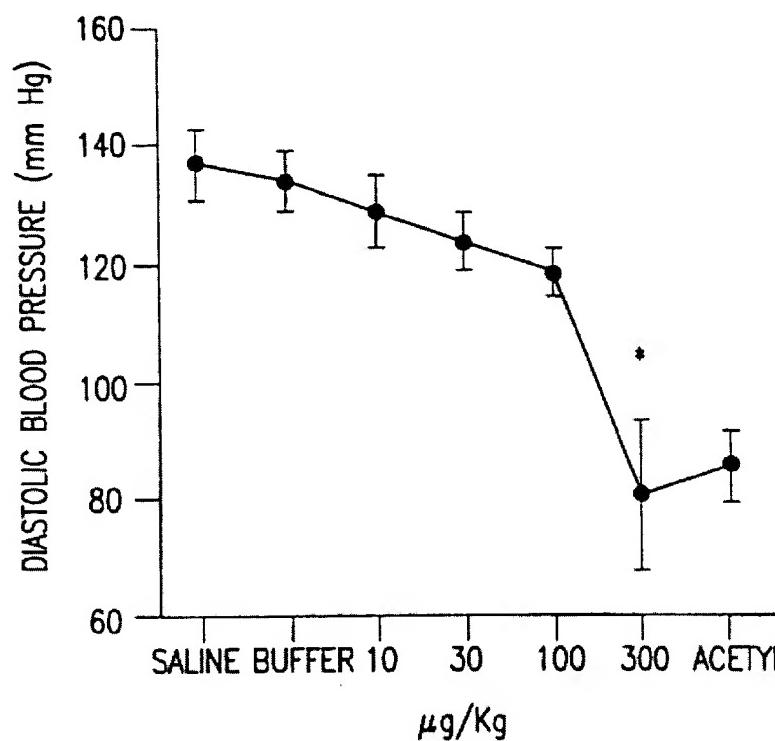


FIG. 26A

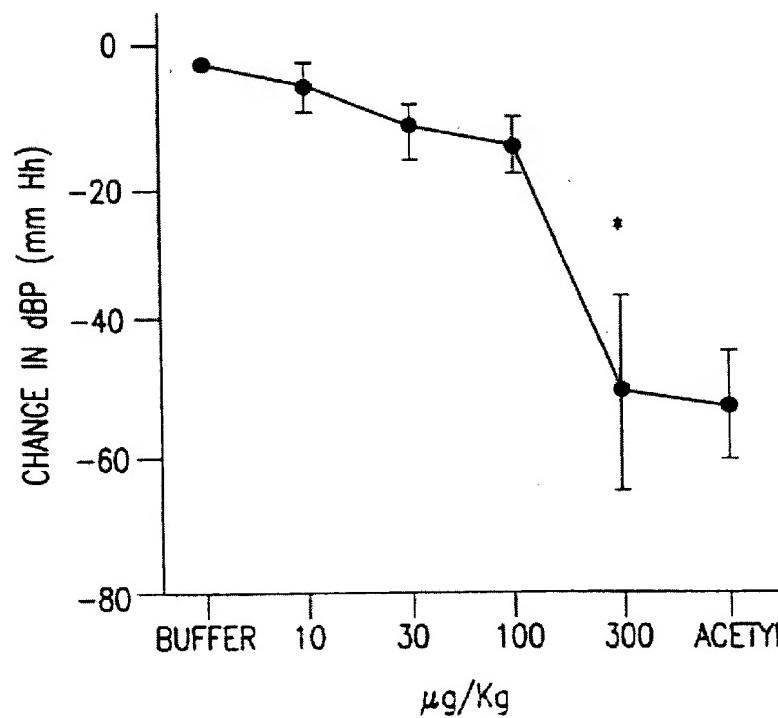


FIG. 26B

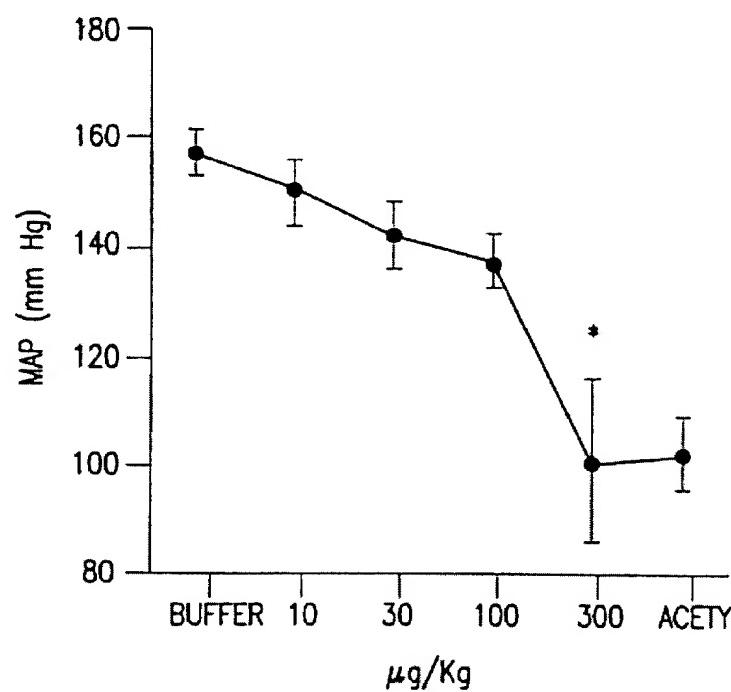


FIG. 26C

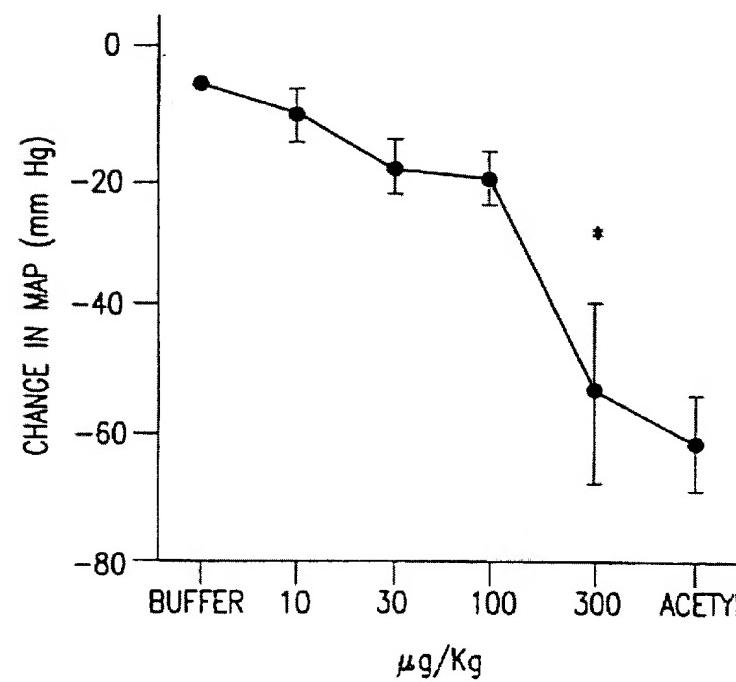


FIG. 26D

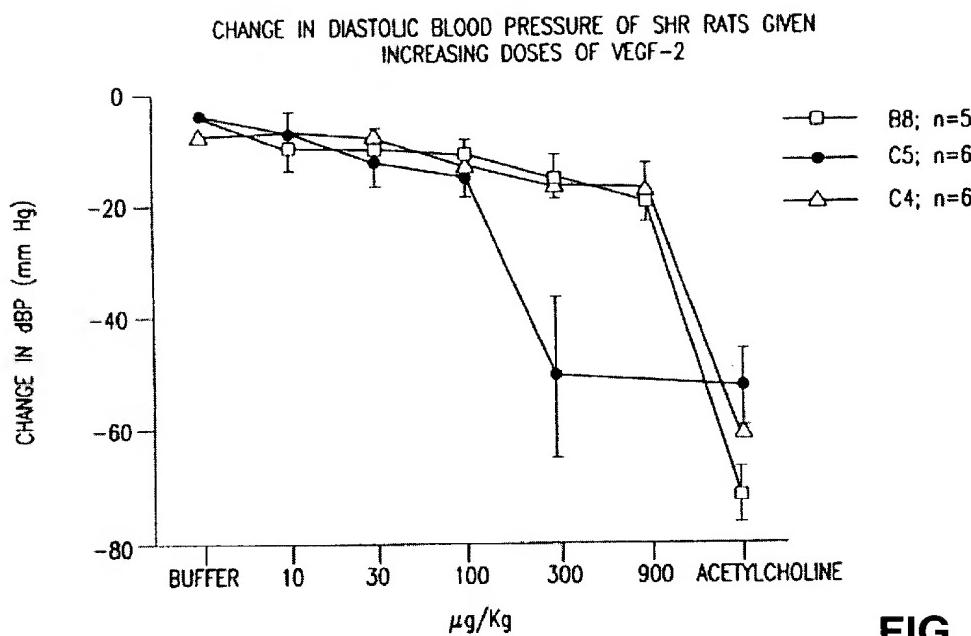


FIG. 26E

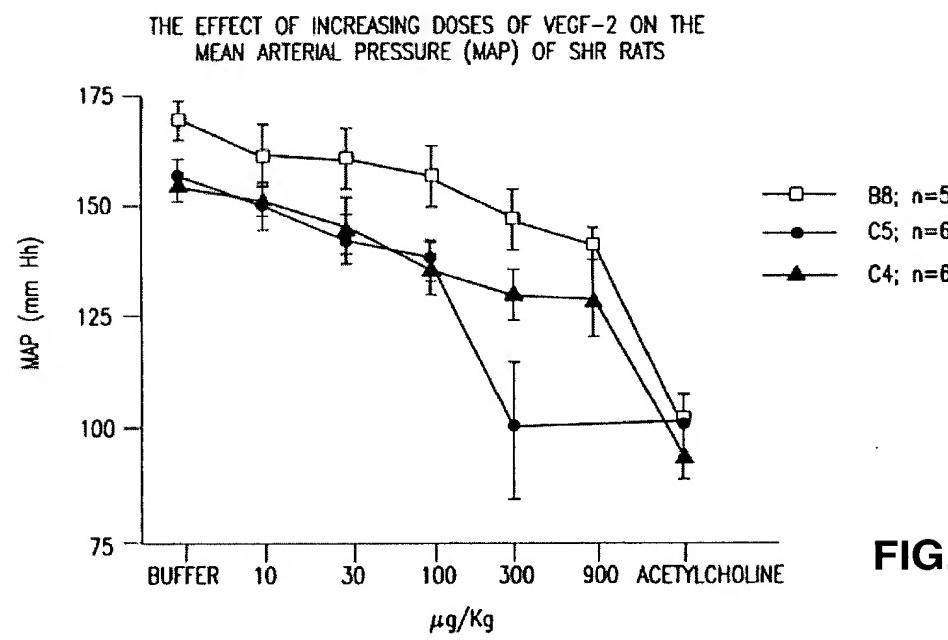


FIG. 26F

THE EFFECT OF VEGF-2 ON THE DIASTOLIC BLOOD PRESSURE OF SHR RATS

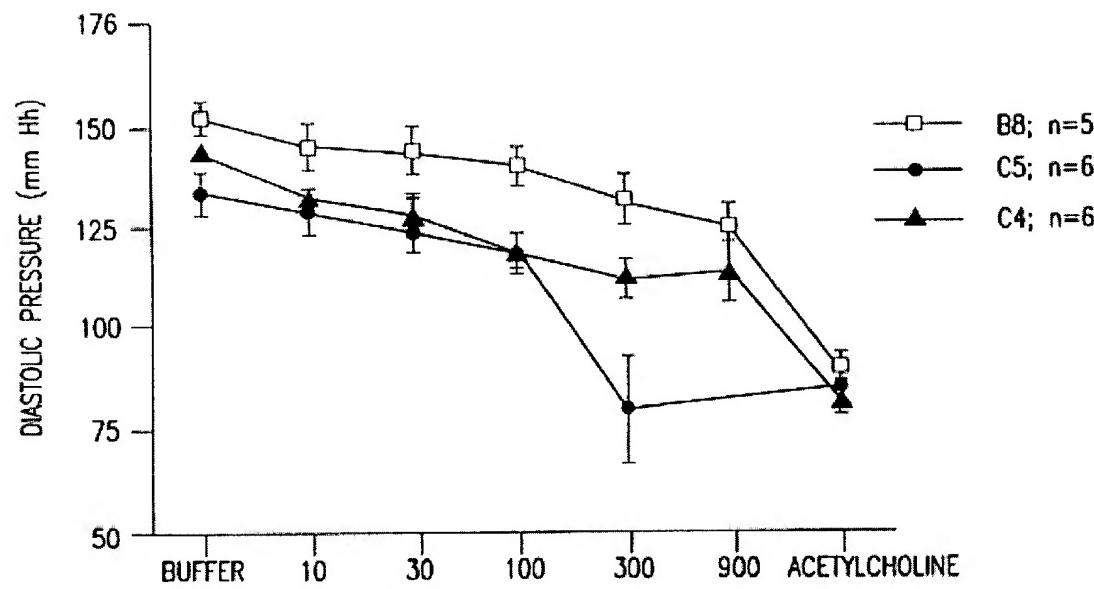


FIG. 26G

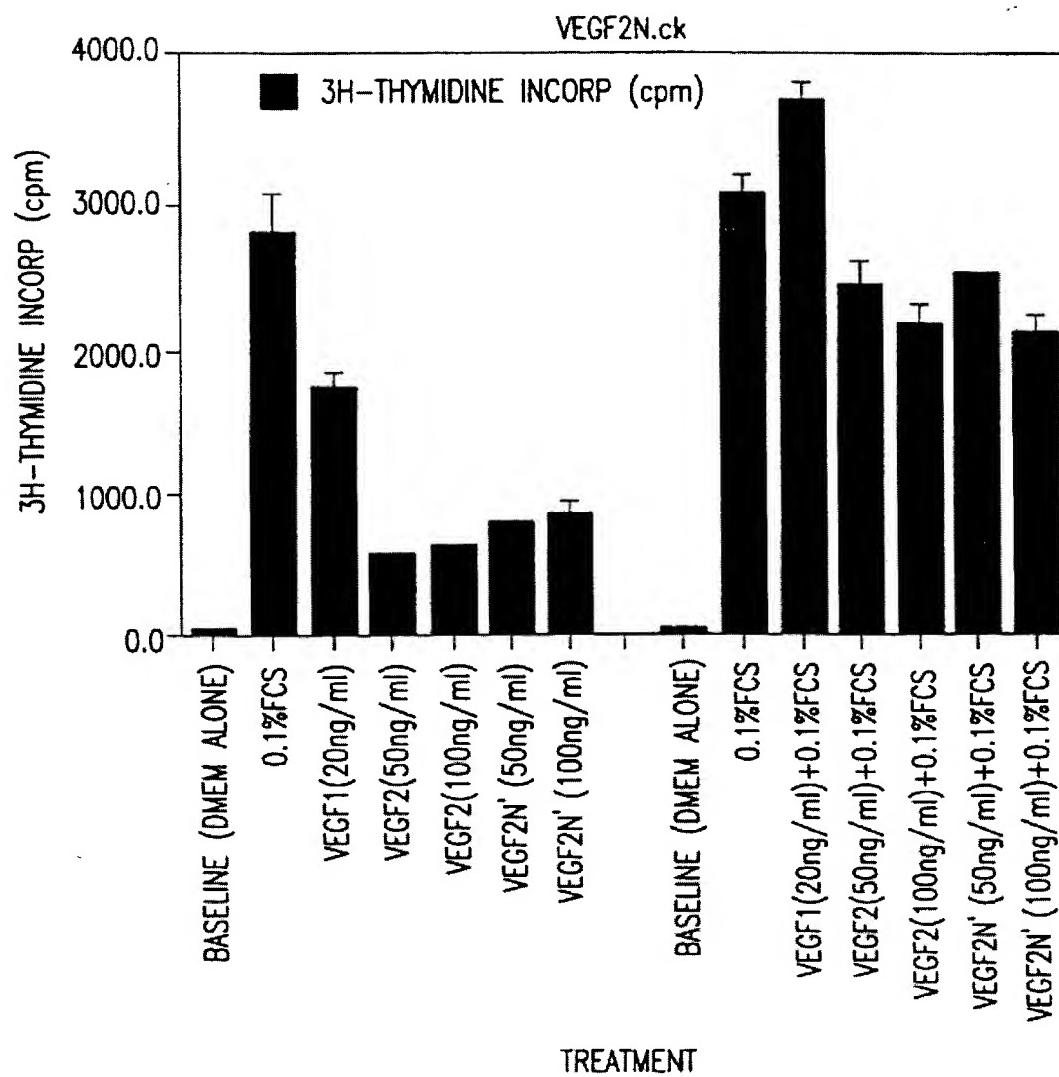


FIG. 27

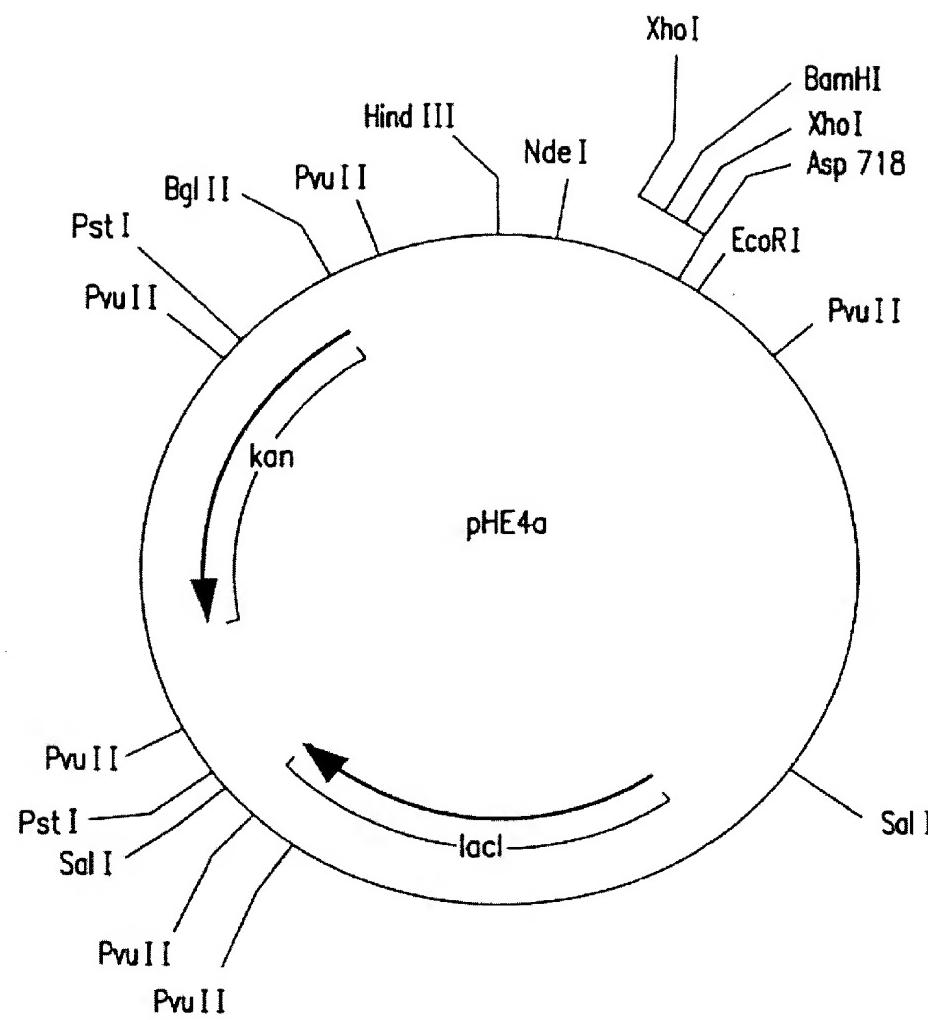


FIG. 28

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LABORATORY

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-35 OPERATOR 1
1 A A G C T T A A A A A A C T G C A A A A A T A G C T T I G A C T T I G T G A G G G A T A A G C A A T

-10 OPERATOR 2
50 T A A G A T G C T A C C C A A T T I G A G G G A T A A C A A T T I T C A C A C A T T A A

S/D
94 A G A G G A A A T T A C A T A T G

FIG. 29

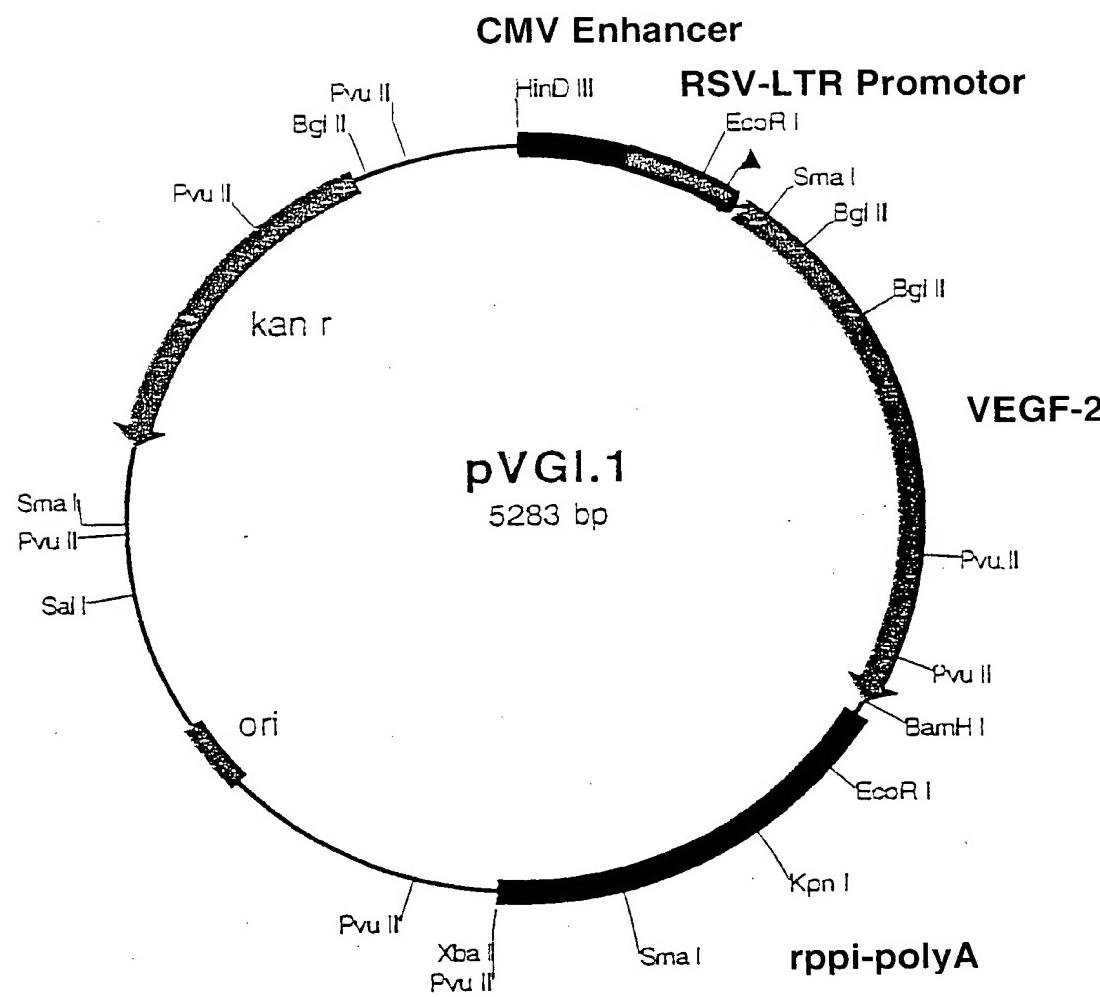


FIG. 30



HindIII

AAGCTT GACCTT ATGCCACTTT CCTACTTGGCAGTACATCTACGTTACGTATTAGTCATCGCTTACCATGGTGATGCC
75
TTCGAACCTGGAAATACCGCTGAAAGGATGAACCGTCATGTAGATAATCGATAATCGATAATGGTACCACTACGC

Ncol

GTTTGGCAGTACATCAATGGGGTTTAGCGGTTTGACTCACGGGGATTCCAAAGTCTCCACCCCCACTGACGT
150
CAAACCCGTCAATGAGTACCCGACCTATGCCAAACTGAGTGCCCCTAAGGTTTCAGAGGTGGGGTACTGCA

CMV Enhancer

CAATGGGAGTTGGCACCAAAATCAACGAGACTTCCAAAATGTCGTAACAACCTCCGCCATTGACCCA
225
GTTACCCCTCAAAACAAACCGTGGTTTAGTTGCTCTGAAGGTTTACAGCATTGAGGGGGTTAACCTGGCT

CMV Enhancer

FIG.31A



AATGGGGCAACATGCTTATGTAACGGTGAGTTAGGAAACATGCCCTATAAGGAGAAAAAGCACCGTG
TTACCCGCCATGCCATTGAGAATACATTGCCACTCAATCGTTGACGGAAATATTCCCTCTTTCTGGCAC
300

The diagram illustrates the vector construct. It features a thick black horizontal bar representing the CMV Enhancer at the bottom. Above it is a thinner black horizontal bar representing the RSV-LTR Promoter. The target gene sequence is shown as a vertical line of text with a dotted line running through it, indicating its orientation. The sequence itself is: CATGCCATTGGGAGTAAGGTGGTATGATCGTGCTTGTAGGAAGGCAACAGACGGGTCTTACCCCCAACCCCATACCTAGCACCAACTAGCACGGAAACAATCCTTCGGTTGTCGCCAGA.

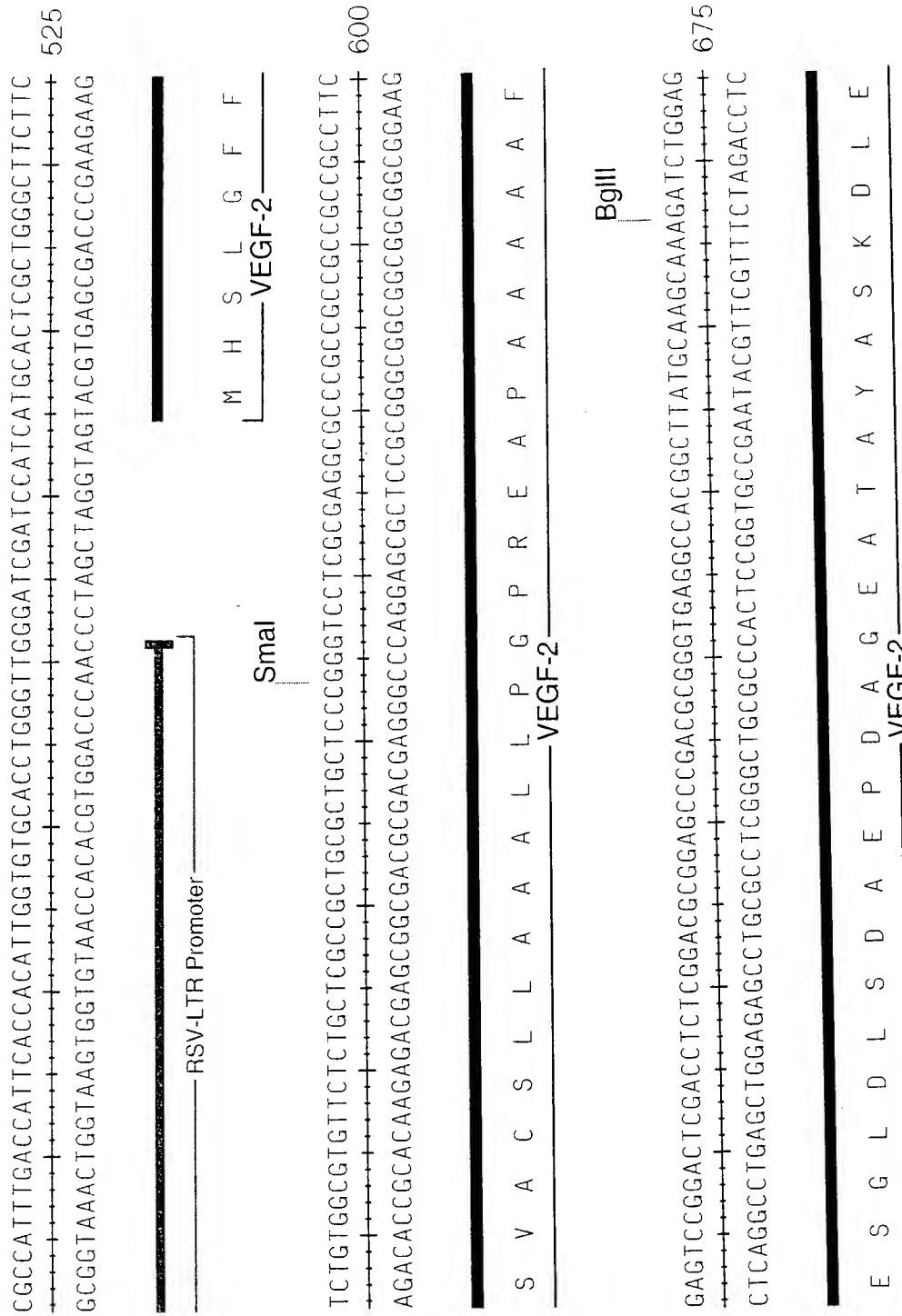
AACACGGATTGGACGAACCACTGAATTCCGCATTGAGAGATATTGTATTAAAGTGCCAGCTCGATAAA
TTTCTCCCTAACCTCTGGGCACTTAAGGCGTAAACGTCCTAAATCAGGGTCGAGCTAATGTTATT
RSV-LTR Promoter

RSV-1TR Promoter

FIG. 31 B



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EIG 31C



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GAGCAGTTACGGCTGTGTCAGTGTAGATGAACCTCATGACTCTACCCAGAAATTGGAAAAATGTACAAG
CTCGCAATGCCAGACACAGGTACATCTACTTGAGTAATGACATGAGATGGGTCTTACATGTT
[REDACTED]

E O L R S V S S V D E L M T V L Y P E Y W K M Y K
[REDACTED] VEGF-2

TGTAGCTAAGGAAAGGAGGCCTGGCAACATAACAGAGAACAGGCCAACCTCAACTCAAGGACAGAGACTATA
ACAGTCGATTCTTCTCCGACCCTTGTATTCGTCCTGGAGTTGAGTTCTGCTCTCTGAT
[REDACTED]

C Q L R K G G W Q H N R E Q A N L N S R T E E T I
[REDACTED] VEGF-2

PstI BglII
AAATTTCGCTGAGCACATTATAACAGAGATCTTGAAAGTATTGATAATGAGTTGGAGAAAGACCTCAATGCATG
TTAACGACGTCGTTGTAATATTATGCTCTAGAACATTACTCACCTCTTGTAGTTACGTAC
[REDACTED]

K F A A H Y N T E I L K S I D N E W R K T Q C M
[REDACTED] VEGF-2

FIG.31D

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CCACGGAGGTGTATAGATGIGGGAAAGGAGTTGGAGTCGGACAAACACCTTAAACCTCCATGTG 975
GGTGCCCTCACACATATCTACACCCCTCAAAACCTCAGCGCTGTTGGAAAGAAATTGGAGGTACAC

P R E V C I D V G K E F G V A T N T F K P P C V
VEGF-2

PstI

TCCGCTACAGATGIGGGTTGCTGCAATAGTGAGGGCTGCAGTGCATGAACACCAGCACGAGCTACCTCAGC 1050
AGGCAGATGCTCACACCCAACGACGTTATCACTCCCGACGTCACGTACTTGTTGGCTGATGGAGTCG

S V Y R C G G C C N S E G L Q C M N T S T S Y L S
VEGF-2

AAGACGTTATTGAAATTACAGTGCCCTCTCTCAAGGCCAAACCAAGTAACAATCAGTTTGCCAAATCACACT 1125
TTCTGCAATAACTTAATGTCACGGAGAGTTCCGGGTTGGTCATTGTTAGTCAAACGGTTAGTGTGA

K T L F E I T V P L S Q G P K P V T I S F A N H T
VEGF-2

FIG.31E



T C T G C C G A T G C T T A A A C T G G A T G T T A C A G A C A A G T C A T T C C A T T A G A C G T T C C T G C C A G C A C A
1200
A G G A C G G C T A C G G T A C A G A T T G A C C T A C A A A T G T C G T T C A A G T A A G G T A A T C T G C A A G G A C G G T C G T T G T

S C R C M S K L D V Y R Q V H S I I R R S L P A T
VEGF-2

PstI

C T A C C A C A G T G C A G G C A G G G A A C A A G A C C T G C C C A C C A A T T A C A T G T G G A A A T A A T C A C A C A T C T G C A G A T G C C T G
1275
G A T G G T G T C A C A G T C C G T C G C T T G T T C T G G A C G G G G T G G T T A A T G T A C A C C T T A T T A G T G T A G A C G G T C T A C G G A C

L P O C Q A A N K T C P T N Y M W N N H I C R C L
VEGF-2

G C T A C G G A A G A T T T A T G T T T C C T G G A T G C T G G G A T G A C T C A A C A G A T G G A T T C C A T G A C A T C T G T G G A C C A
1350
C G A G T C C T T C T A A A A T A C A A A A G G A G C C T A C G A C C T T A C T G A G G T T A C T G A G G T A A G G T A C T G T A G A C A C C T G G T

A Q E D F M F S S D A G D D S T D G F H D I C G P
VEGF-2

FIG.31F



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Pvul

B51

AACAAGGAGCTGGATGAAGAGACCTGTCACTGTCAGTGTCTGGAGAGGGCTGGCTGGAGCTGGACACCTGGGGTG
1425

N K E L D E E T C O C V C R A G L R P A S C G P H

AAAGAACTAGACAGAAACTCATGCCAGTGTGCTGTAAAACAAACTCTTCCCAGCCAAATGTGGGCAACCGA
+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
TTCTTGATCTGTGCTTGAAGTACGGTCACACAGACATTITGAGAAAGGGTGTGGTTACACCCCCGGTTGGCT

K E L D R N S C Q C V C K N K L F P S A C G A N R

GAATTGAAACACATGCCAGTGTATGAAAGAACCTGGCCAGAAAATCAACCCCTAAATCCTGGAAAAT
CTTAAACACTACATTTCTTGACGGTACACATACTACATTTCTTGACGGGTCTTATGTGGGGATTAGGACCTTT

E F D E N T C Q C V C K R T C P R N Q P L N P G K
VEGF-2

FIG. 31 G



Pvull

TGTGCCCTGTTGAATGACAGAAAGTCCACAGAAAATGCTTGTAAAAAGGAAAGAAGTTCCACCAAAACATGCAGC
ACACGGACACTTACATGCTTCAAGGTGTCCTTACGAACATAATTCCCTTCAAGGGGGTTGTACGTCG
1650

C A C E C T E S P Q K C L .K G K F H H Q T C R
VEGF-2

BamHI

TGTACAGACGGCCATGTTACGAACCGCCAGAACGGCTTGAGGCCAGGGATTTCATATAGTGAAGAACAGTGTGTCGT
ACAATGTCGCCGGTACATGCTTGGCGGTCTCGAACACTCGGTCTAAAGTATACTCTTACACAGCA
1725

C Y R R P C T N R Q K A C E P G F S Y S E E V C R
VEGF-2

FIG.31H



AGCACCTTTGGTTCTCACTTGGTGGAAAGCTCTACCTGGTGTCACACACCCCA
1875
TCGTGGAAACACCAAGAGTGAACCACCTTGAGAGATGGACACACACCCCTGGACCTAAGAAGATGTTGGGT

rppi poly A

TGTCCCCGCCGAAGTGGAGGACCCACAAGGTAAGCTTGCTCTGAAATTCTTCAACTACCCCTGT
1950
ACAGGGGGGGCTTCACTCTGGGTGTCCATTGAGACGAGGACTTAAGATAAGGTTCACGATTGATGGGACA

rppi poly A

TTGTCTTCAACCTTGAGACCTTGTAAAATTGTGCCCTAGGTGGAGGGCTCAGGCTAACCAAGTGGGGGCACA
2025
AACAGAAAGTGGAAACTCTGGAACATTAAACACGGATCCACACCTCCCAGAGTCGGATGGTCACCCCCGGTGT

rppi poly A

FIG. 31I

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TTTCCTGGCAGCTAGACATATGTAACATGGTAGCTGCAGGAAGGAGTGAAGAATCCCTTAAGTCCTCA 2100
AAAGACACCCCGTGTGATCTGTATACTTGTACCATCGACGGTCCCTCACTCTTAGGAAGGAATTCAAGGAT

rppi poly A

KpnI

GGTGGTGACGGGTGGCTAGGCCAGGATAGGTACCTATTGGGACCCATAGAGCAGTGCACGTGACTGAGGGA 2175
CCACCACTGCCAACCGATCCGGGTCCATCCATGGATAAACCCC TGGGTATCTCGTGACGTGACTCCCT

rppi poly A

TGGTAACAGGATGTGTAGGTTTGGAGGCCATATGTCATTGACCTGGTACCTGCTCACAGCCATGCAAC 2250
ACCATTGGCTCACACATCCAAAACCTCCGGGTATACAGGTAAAGTACTGGTACACTGAAAGAGTGTGGTACGTG

rppi poly A

FIG.31J



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CCTTGCTCTGTGCTGACTTAGCAGGGATAAAAGTGAGAGAAAGCCCTGGGCTTAATCAGGGGGTGCCTCAGTC
GGAACGGAGGACACCGACTGAATCGTCCCTCATTTCACTCTTGGACCCGATTAGTCCCCAGGGAGTCAGG
2325

rppi poly A

TCCTTAACTGGATTCTATGGTCTTGTGCTGCTGCTTGCTTGCTTGCTTGCCCTTGCTGACATGACCTCCTG
AGGATTGACCTAACAGGATAACAGAAAAGAACACGGACACTAGAGACGGACACGGACTGACTGGAGGGAC
2400

rppi poly A

SmaI

GCAGTGGCACAACTGGAGCTGGGTGGAGGCCGGGGCAGGTGACCTTCAGACCTTGGAACCTGGGACTGGAGGTGGCCGG
CGTCACCGTGTGACCTGGACCCACCTGGGGCCCGTCCACCTGGAAAGTCIGGAACCGTGGACCTCCACGGGCC
2475

rppi poly A

CAGAAGCGGGCATCGTGGATCAGTGCTGCACCAAGCATCTGCTCTTACCAAACCTGGAGAAACTACTGCAACTAG
GTCTTGGCCGTAGCACCTAGTCACGACGTGGCTAGACGAGAGATGGTTGACCTTGATGACGTTGATC
2550

rppi poly A

FIG.31K



GGCCACCACTACCCCTGTCCACCCCTCTGCAATGAATAAACCTTTGAAAGAGCACTACAAGTTGAGTGTACATGC
CGGGTGGTCAATGGGACACAGTGAGGAGACGTTACTTATTTGGAAACTTTTCGGTGTGTTAACACACATGTACG 2625

[REDACTED]

[REDACTED] rppi poly A

GTGCATGTGCATATGTGGTGGGGGGAAACATGAGTGGGGCTGGCTGGAGTGGTGGCTGGCTTAATCTATCTGGCA
CACGTACACGTATACACCACGCCCTTGTACTCACCCCGACCGACCTCACACAGGCCGAATTAGATAACCCGT 2700

[REDACTED]

[REDACTED] rppi poly A

PvuII XbaI

GCTGTCTAGACGTAATCATGGTCAAGCTGTGTTCTGTGAAATTGTTATCCGCTCACAAATTCCACACATA
CGACAGATCTGCATTAGTACCAAGTATCGACAAAGGACACACTTAAACAAATTAGGCCAGTGTAAAGGTGTGTGTAT 2775

CGAGGCCGGAAAGCATAAAGTAAAGCCTGGGGTGCCTAATGAGTGAAGCTAACCTCACATAATTGCGTTGCCGCTCA
GCTCGGCCCTTCGTATTTCACATTGGACCCACGGATTACTCACTCGATTGAGTGTAAATTAAACGCCAACGGAGT 2850

FIG.31L



PvuII

CTGGCCGCTTTCCAGTGGAAACCTGTCTGCCAGCTGCATTAAATGAAATCGCCAACGGCGGGAGAGCCGT
GACGGCGAAAGGTCAGCCCTTGACAGCACGGTCGACGTAAATTACTTAGCCGGTTGGCCTCCGCCAT

TTGCGTATTGGGGCTCTTCCGGCTCGCTCACTGACTCGCTGGCTCGGTGTTGGCTGCGGAGGGTA
AACGCATAACCCGGAGAGGAAGGGCAAGGGCAGCGGAGCTGAGCTGAGCTGAGTGGCTTGTACACTGGTTT

TCAGCTCACTCAAAGGGGTAATAACGGTTATCCACAGAAATCAGGGATAACGGAGAAACATGTGAGCAAA
AGTCGAGTGAGTTCCGCCATTATGCCAATAGGTGCTTAGTCCCATTATGCCCTTATGGCTTGTACACTGGTTT

GGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGGCTGGCTGGCTTTCCATAGGCTCCGCCCTGACGGAG
CCGGTCTGGTTCCGGICCTTGGCATTTTCCGGCAACGACGGCAAAAGGTATCCAGGGGGGACTGCTC

FIG. 31M



CATCACAAATACTGACGCCTCAAGTCAGAGGTGGCGAAAACCCGACAGGACTATAAAGATAACCAGGGTTTCCCCCT
GTAGTGTGTTTAGCTGGAGATCAGTCAGTCACCCGCTTACGGATACCTGTCGGCTTCCCTTCTCCCTGGGA
3225

GGAAAGCTCCCTCGCGCTCTGCTGGACCCCTGCCGCTTACCGGATACCTGTCGGCTTCCCTTCTCCCTGGGA
CCTTCAGGGAGCACGGAGAGGACAAGGGCTGGGACGGGAATGGCCTATGGACAGGGAAAGAGGGAAAGCCCT
3300

AGCGGTGGCTTTCTCATAGCTCAGCTGAGGTATCTCAGTTCGGTAGGTCGTTGGCTCCAAAGCTGGCTGT
TCGCACCGCGAAAGAGTATCGAGTGCAGACATCCATAGAGTCAGGCTAACGCAAGCCACATCCAGGAGGTTCGACCCGACA
3375

GTTGACGAAACCCCCGGTTCAAGCCCCGACCGCTGGCTTATCCGGTAACATCGTCTTGAGTCACCCGGTAAGA
CACGTGCTTGGGGGCAAGTCGGGACGGAAATTAGGCCATTAGGCAAGAACTCAGGTTCAGGTTGGGCCATTCT
3450

CACGACTTATCGCCACTGGCAGGCCACTGGTAACAGGATTAGCAGGGAGGTATGTTAGGGGGCTACAGAG
GTTGCTGAATTAGGGGTGACCGTGGTGACCATTTGTCCTTAATCGTCCTGCTCCATACATCCGCACGATGTC
3525

FIG.31N



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TCTTGAAGTGGGCCAACTACGGCTACACTAGAAAGAACAGIATTGGTATCTGGCTCTGGCTGAAGCCAGTT
3600
AAGAACCTTCAACCACCGGATTGATGCCGATGTGATCTTGTICATAAACCATAGACCGAGACCTCGGTCAA

ACCTTCGGAAAAAGAGTTGGTAGCTTTGATCCTGGATCCTTAAGAACCAACCCGCTGGTAGCGGTGGTTTGTTCAG
3675
TGGAAGCCTTTTCTCAACCATCGAGAACCTAGGCCGTTTGTGGCGACCATGCCACCAAAAAAACAAACCG

AAGCAGCAGATTACGGCAGAAAAAAAGGATCTCAAGAACGATCCTTGTATCTTGTACGGGTCTGACGCTCAG
3750
TTCTGCCTTAATGCCGCTTTCTAGAGTTCTAGAAACTAGAAAAGATGCCACAGACTGCGAGTC

Sall

TGGAACGAAAACCTACGGTTAACGGATTGGTCATGAGATATGGTACGGACCAAGGGCCATCGTGCCTCCCCAC
3825
ACCTTGCTTTGAGTGCATTCCCTAAACCAATTCTAATAGCAGCTACTCTAACTCTAATAGCAGCTGGTTGCCGGTAGCACGGAGGGTG

FIG.31O

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PstI |
TCCTGCAGTTGGGGCATGGATGCCGATAGCCGCTGCTGGTTTCTGGATGCCGACGGATTGCACTGGCGG
3900
AGGACGTCAAGCCCCGGTACCTACGCCCTATGGGCCATACGGCTAACGGCTAACACTAAACGTTGACGGCC

PvuII |
TAGAAACTCCGGGAGGTGTCAGGCCCTCAGGCAGGCTGAACCAACTCGCGAGGGATCGAGGCCGGGGTGGCG
3975
ATCTGAGGCCGCTCCAGCAGGTGGAGTCGGCTCGACTTGGTTAGGCCTCCCTAGCTCGGGCCCAUCCGC

SmaI |
AAGAACTCCAGCATGAGATCCCGGGCTGGAGGATCATCCAGCCGGCTCCGGAAAACGATTCCGAAGCCCCAAC
4050
TTCTTGAGGGTGTACTCTAGGGGGCGGACCTCCCTAGGGTGGGGCTTTTGCTAAGGCTTGGGTTG

CCTTCATAGAAGGGGGTGGAAATCGAAATCTCGTGAATGGCAGGTGGGGCTCGCTGGTCAATTGAAAC
4125
GAAAGTATCTTCCGGCCACCTTAGCTTAGAGCAC TACCGTCCAAACCCGAGCCAGTAAAGCTTG

FIG.31P



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F F E D L L R Y F A I R Q S D P A A I G

CGTAAAGCACGAGGAAGGGTCAGCCCATTGGCCCAAGCTCTTCAGCAATATCAGGGTAGCCAACGGCTATGT
GTTATGGCTCTTGCCAGTCGGTAAGGGGGITCGAGAAGTGTATAGGCCCATCGTTGGGATAACA
4275

Y L V L F R D A W E G G L E E A I D R T A L A I D

CCTGATAGCGGTCCGCCACACCCAGCCCCACAGTCGATGAATCCAGAAAAGGGCATTTCACCATGATA
GGACTATGGCAGGGGGTGGGTGGGGTGGTCACTTAGGTCTTTCCGGTAAAGGTGGTACTATA 4350

Q Y R D A V G L R G C D I F G S F R G N E V M I N
kan

FIG.31Q



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Ncol

TCGGCAAGCAGGATGCCATGGGTACCGAGAGATCGCCGTCGGCATGGGCCTTGAGCCGGGAACA
4425
AGCCGGTCCGTCCGTAGGGTAGCCAGTAGCTGCTCTAGGAGGGCAGCCGTACGGCGGAACACTCGGACCGCTTGT

P L C A D G H T V V L D E G D P M R A K L R A F L
kan r

GTTCCGGCTGGCGGAGGCCCTGATGCTCTTCTGTCAGATCATCCTGATCGACAAGACCGGCTTCGAGTAC
4500
CAAGCCGACCCGGCTCGGGGACTACCGAGAACCTAGGACTAGCTGTTCTGGCCAAAGGTAGGGCTCATG

E A P A L G Q H E E D L D Q D V L G A E M R T R
kan r

GTGCTCGCTCGATGCGATTGGCTGGTGAATGGCGAGTAGCCGGATCAAGCGTATGAGGCCGGCA
4575
CACCGAGCGAGCTACGGCTACCGACTACAAAGGAACCAACCAGCTTACCCGTCCTAGTTGGCATACGGTGGCGGT

A R E I R H K A Q H D F P C T A P D L T H L R R M
kan r

FIG.31R

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TTGCATCAGCCATGGATACTTTCGGCAGGCAAGGTGAGATGACAGGAGATCCCTGCCCGGCACCTTCGC
AACGGTAGTCGGTACTACCTATGAAAGAGCCGCTCCTCGTTCCACTCTACTGTICCTCTAGGACGGGGCGTGAAGCG

A D A M I S V K E A P A L H S S L D Q G P V E G
kan r

Pvull

CCAATAGCAGCCAGTCCTTCCCGCTTCAGTGACAACGTCGGCAGGACAGCTGCCAAAGGAACGCCCGTCACTGGCCA
GGTTATCGTCGGTCAGGGAAAGGGCAAGTGACTGTTGCAGCTCGTGTGACGGCTTCCTTGCGGGCAGCACCGGT

L L L W D R G A E T V V D L V A A C P V G T T A L
kan r

FIG.31S



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PstI

GGCACGATAGCCGCCTGCCCTCGCTTCAGTTCAACGGGACAGGTGGTCTTGACAAAAAGAACCG
CGGTGCTATGGCGCGACGGAGGACTCAAGTAAGTCCCCTGGCCTGGCCAGAACTGTGTTTCTGGC

W S L R A A E D Q L E N L A G S L D T K V F L V P
kan r

GGCCGCCCTGGCTGACAGCCGGAACACGGGGCATCAGAGCAAGCCGATTGGCTGTGTTGGCCAGTCATAGCCGA
CCGGGGGACGGGACTGTGGCCCTGGCCCTGGCTAACAGACAACAGGGTCAGTATCGCT

R G Q A S L R F V A A D S C G I T Q Q A W D Y G F
kan r

ATAGCCCTCCACCCAAGGGGGGGGAACCTGGGTGCAATCCATCTTGTCAATCATGGGAAACGATCCTCATC
TATGGAGAGGTGGTTGGCGCTCTGGACGGCACGTTAGGTAGAACAAAGTTAGTACGGCTTGGCTAGGAGTAG

L R E V W A A P S G A H L G D Q E I M
kan r

FIG.31T

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BgIII

CTGCTCTTGTATCAGATCCCTGGCCATCAAGATCCCTGGGGCAAGAAAGCCATCCAGTTACTTGC
GACAGAGAACTAGTCTAGAACCTAGGGGACCGGTAGTCAGGAACCCGTTCTGGTAGGTCAAATGAAACG
5025

PvuII

AGGGCTTCCCCAACCTTACCAAGAGGGCCCCAGCTGGCAATTCCGGTTGGCTTGCTGTCCATAAAACCGCCCCAGT
TCCCAGAAGGGTTGGAAATTGGTCTCCCGGGTGCACCGTTAAGGCCAAGCGAACGACAGGTATTGGGGTCA
5100

CTAGCTATCGCCATGTAAGCCCCACTGCAAGCTACCTGCTTCTCTGGCTTTGGCTTTCCCTTGTCCAGATA
GATCGATAGCGGTACATTGGGTGACCTTGATGGACGAAAGAGAAACGGCAACGGAAACAGGTCTATC
5175

CCCAGTAGCTGACATTCACTCCGGGTCAAGCACCGTTTGGCTTCTACGTTGTTGGCTTCCCTTGTAGC
GGGTATCGACTGTAAGTAGGCCCAAGTGTGGCAAAAGACGGCTGACGGAAAGAGATGGCACAGGGGAAGAAATCG
5250

AGCCCTTGGCCCTGAGTGCTTGGGGAGCGGTG
TCGGGAACGGGGACTCACGAACGCCGTGGCAC
5283

FIG.31U